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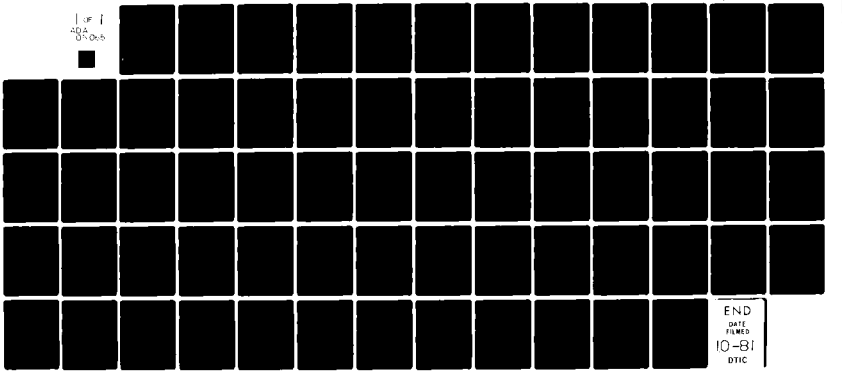

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This project was designed to serve as the first step to examine various aspects of gas exchange during high sustained gravitational stress (HSG) and the influence of commonly used protective measures on the gas exchange process during HSG. Studies focused on four aspects of the problem: 1) Effects of G-suit abdominal bladder inflation on oxygen delivery at +1Gz 2) Interaction of pulmonary mechanics and G-suit bladder inflation during +Gz stress 3) Time course of gas exchange detriment during +Gz stress and the influence of G-suit abdominal bladder inflation on that detriment 4) Use of Krypton-81m

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as a means of examining continuously the topographical distribution of ventilation.

Results in canine studies indicate that, while the G-suit abdominal bladder helps maintain oxygen delivery at low +Gz levels, its use at higher +Gz levels contributes to the gas exchange detriment. The increased detriment is associated with regional lung compression resulting from abdominal bladder inflation. Data indicate that exposure to HSG with G-suit abdominal bladder inflation is sufficient to cause atelectasis even though the subject breathes air.

Effects of Anti-G Measures on Gas Exchange
Final report -- 1 April 78 to 31 May 81

Background

High sustained gravitational stress (HSG), such as that experienced by pilots of high performance aircraft, affects cardiovascular and respiratory function adversely (Burton et al., 1974). Cardiovascular function is compromised because of changes in hydrostatic relationships caused by the increased G. Similar mechanisms influence distribution of ventilation and pulmonary perfusion (Bryan et al., 1966; Jones et al., 1969; Glaister, 1970a; von Nieding and Krekeler, 1973). In addition, the HSG may alter chest wall mechanics (Hershgold, 1960) and impair gas exchange. A number of protective measures are presently employed in an attempt to restore normal arterial blood pressure and, thus, increase pilot tolerance to high sustained gravitational forces. Some of these measures (e.g. anti-G suits) have been associated with additional detriment to pulmonary gas exchange (Barr, 1962; Nolan et al., 1963; Hyde et al., 1963), whereas others (e.g. positive pressure breathing) may enhance pulmonary gas exchange under HSG conditions. Review of the literature reveals little information concerning the effects of standard anti-G measures on gas exchange. In view of this, several questions relevant to HSG tolerance must be answered if more effective protective measures are to be developed:

1. To what extent do commonly used protective measures enhance or impair pulmonary gas exchange?

2. What is the time course of any gas exchange detriment resulting from use of protective devices (e.g. anti-G suits) during HSG?

3. Is there a cumulative effect associated with gas exchange detriment resulting from use of protective devices?

4. By what means can these measures be modified to optimize gas exchange during HSG?

This project was designed to serve as the first step to answer the above questions. Studies have focused on four aspects of the problem; effects of G-suit abdominal bladder inflation on oxygen delivery at +1Gz, interaction of pulmonary mechanics and G-suit inflation during +Gz stress, time course of gas exchange detriment during +Gz stress and the influence of g-suit abdominal bladder inflation on the detriment, and use of Krypton-81m as a means of examining continuous topographical distribution of ventilation.

I. Effects of G-suit abdominal bladder inflation on oxygen delivery at +1Gz

When assessing tolerance to HSG stress, vision impairment is often used as an indicator of oxygen delivery to the brain. Although the anti-G suit abdominal bladder has been shown to increase HSG tolerance (Lewis, 1955; Burton and Krutz, 1975; Burton et al., 1973), its effect on oxygen delivery (cardiac output and arterial oxygenation) during air breathing has not been investigated in the same preparation. The purpose of this study was to quantitate the effects of the G-suit abdominal bladder on oxygen delivery in anesthetized dogs spontaneously breathing room air while exposed to +1Gz stress.

Methods

Adult mongrel dogs of both sexes weighing 20.3 $\pm$ 2.6 Kg were anesthetized with pentobarbital sodium (30 mg/Kg) and intubated with a cuffed endotracheal tube. A catheter was placed in the carotid artery for blood sampling and arterial blood pressure monitoring, and a 7 French thermal dilution Swan-Ganz catheter was introduced into the pulmonary artery and right atrium via the external jugular vein for blood sampling and thermal dilution cardiac output determination. Body temperature was monitored with a thermistor placed in the esophagus. A 10 cm wide inflatable tourniquet cuff was placed around the animal's abdomen to simulate the G-suit abdominal bladder. The animal was then placed in a head-up, vertical position (+1Gz), and the endotracheal tube was connected to a Rudolf valve arranged so that expired gas passed through a heated pneumotachograph and a gas mixing chamber. The pneumotachograph signal was integrated to provide a measure of minute

ventilation, and the carbon dioxide tension at the outlet of the mixing chamber was monitored. All recordings were made on an 8-channel polygraph.

Ten minutes after the animal had been placed upright, arterial and mixed venous blood were sampled for blood-gas analysis, and cardiac output was determined. The abdominal bladder was then inflated to 100 Torr (approximately 2 psi). Ten minutes after bladder inflation, arterial and mixed venous blood gas composition and cardiac output were again determined. The bladder was deflated, and the process was repeated.

Results

Results from 28 trials in 10 animals are shown in Table I-1. Adjacent trials were compared with a paired t-test. An 8% increase in oxygen delivery was observed when the bladder was inflated ($P<0.05$). The increase in oxygen delivery resulted from an increased cardiac output that accompanied bladder inflation ($P<0.02$). No difference in arterial oxygen content was observed.

To estimate the time course of the cardiac output change, determinations in 4 animals were also made one minute after bladder inflation or deflation. Results from these experiments are shown in Figure I-1. In these animals, the cardiac output change occurred within one minute after bladder inflation or deflation.

Discussion

The dog, in its normal posture, experiences the influence of gravity in the -Gx direction. Hence, placing the animal in a vertical,

TABLE I-1. EFFECTS OF ABDOMINAL BLADDER IN DOGS AT +1Gz

BLADDER PRESSURE (TORR)	OXYGEN DELIVERY (ML/MIN)	=	CARDIAC OUTPUT (L/MIN)	X	ARTERIAL OXYGEN CONTENT (ML/100ML)	MINUTE VENTILATION (ML/MIN)	PER CENT DEAD SPACE	PER CENT VENOUS ADMIXTURE
0	495		2.34		20.6	4685	38.5	9.22
(SEM)	216		0.79		3.07	492	1.69	1.01
100	535		2.60		20.4	4897	38.3	8.42
(SEM)	213		0.77		3.42	564	2.28	0.71
	$P<.05$		$P<.02$		NS	NS	NS	NS

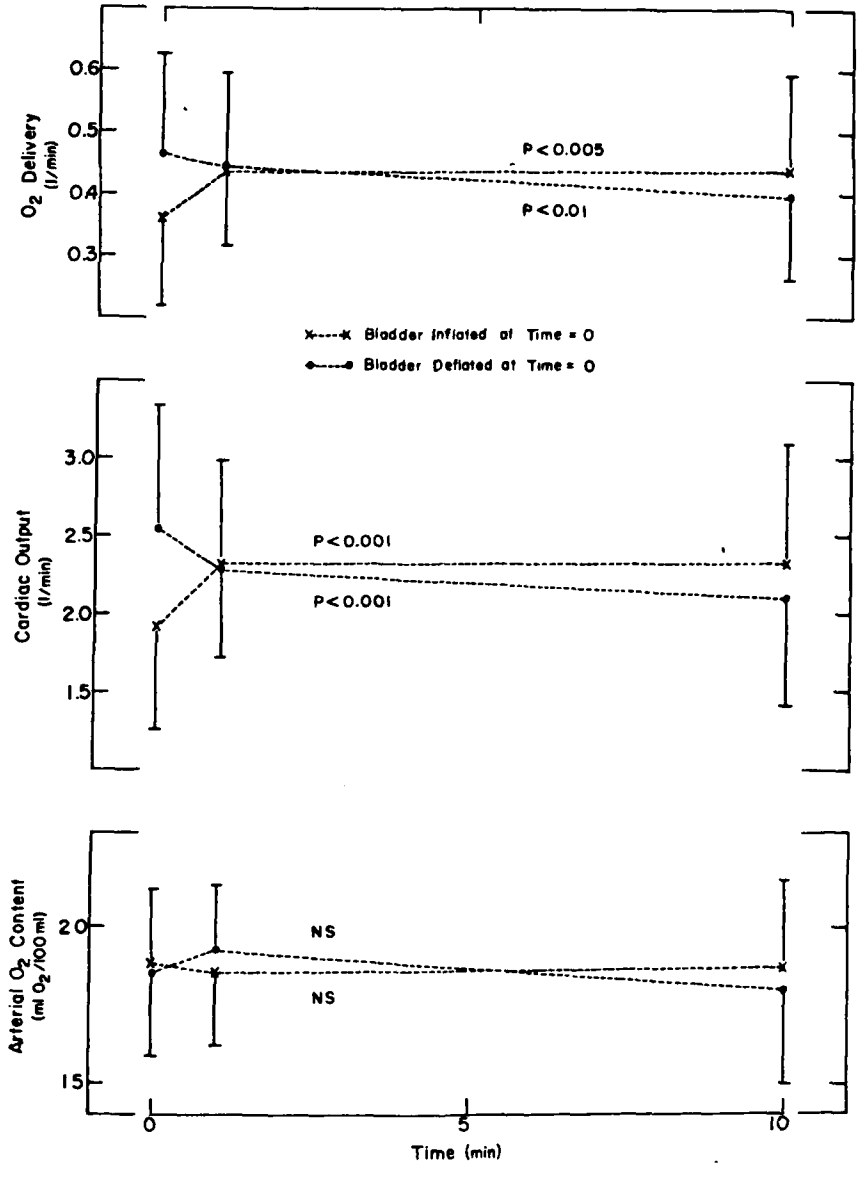

Figure I-1. Oxygen delivery, cardiac output and arterial oxygen content one and 10 minutes after abdominal bladder inflation or deflation in 4 dogs exposed to +1 Gz stress. P values refer to results of F-test testing for differences in each three point set. Bars indicate standard error of the mean.

head-up position (+1Gz) exposes it to a greater physiological G stress than does a similar posture in man. Lindberg et al. (1960) examined the cardiovascular effects of G-suit inflation in men exposed to +2,3 and 4 Gz and concluded that G-suit inflation did not change cardiac output significantly. Sackner and Wanner (1976) re-examined the influence of G suit inflation on cardiac output. They focused on the manner in which the G-suit was inflated. Cardiac output in man breathing air at +1Gz when the standard G-suit inflation scheme (abdominal bladder followed by leg bladders) was followed was compared with that measured when the G-suit was inflated upwards (leg bladders, then abdominal bladder). Cardiac output did not change when the standard scheme was followed. However, when the leg bladders were inflated first, cardiac output increased significantly. Their results suggest that, by inflating the leg bladders first, less blood pooling occurred in the legs, and central volume increased. Because the dog has relatively little muscle mass in its legs, most blood pooling during +Gz stress would occur in the abdomen, and bladder inflation would reduce pooling. Data from this study support this hypothesis. Inflation of the abdominal bladder during +1Gz stress resulted in a higher cardiac output.

G-suit inflation has been implicated as one key factor necessary for acceleration atelectasis development (Glaister, 1970b). On this basis, we would have expected bladder inflation to promote spontaneous atelectasis in dependent lung regions thereby causing arterial desaturation. Arterial oxygenation, however, was not affected in our study when the bladder was inflated. To obtain an indication of changes in distribution of ventilation following bladder inflation or deflation, the topographical distribution of ventilation was assessed in two

animals using Krypton-81m. Krypton-81m is a high energy isotope having a half-life of 13 seconds. Because of its short half-life, the activity measured over the lung during continuous Krypton-81m inhalation is proportional to ventilation (see Study IV). Hence, distribution of ventilation can be examined "dynamically" relative to other isotope techniques. While the procedure outlined above was being followed, the animal inspired from a reservoir into which air and Krypton-81m were mixed continuously. Using a left lateral view of the lungs, Krypton activity was monitored with a G.E. high resolution portable gamma camera and associated computer equipment. Fifteen second Krypton images were acquired for 2 minutes prior to bladder inflation or deflation and 2-3 minutes following bladder inflation or deflation. Results were similar in both dogs. Figure I-2 shows the distribution of Krypton activity, expressed as per cent total counts over the lung, to one region near the lung apex and another near the lung base in one of the animals. When the bladder was inflated, ventilation increased to the apex (X, upper panel) and decreased to the base (X, lower panel) ($P<0.005$, unpaired t-test). This pattern was reversed when the bladder was deflated (O) ($P<0.005$). Despite the redistribution of ventilation, no change in physiological dead space or venous admixture occurred (Table I-1). Hence, a redistribution of blood flow must have also occurred.

Ross and his colleagues (1962) and Sackner and Wanner (1975) measured higher diffusing capacities in man with G-suit inflation. Since the diffusing capacity test reflects the pulmonary capillary blood volume, such an increase indicates increased pulmonary vascular volume or a more even distribution of perfusion.

Barr, Bjurstedt and Coleridge (1959) monitored arterial oxygen

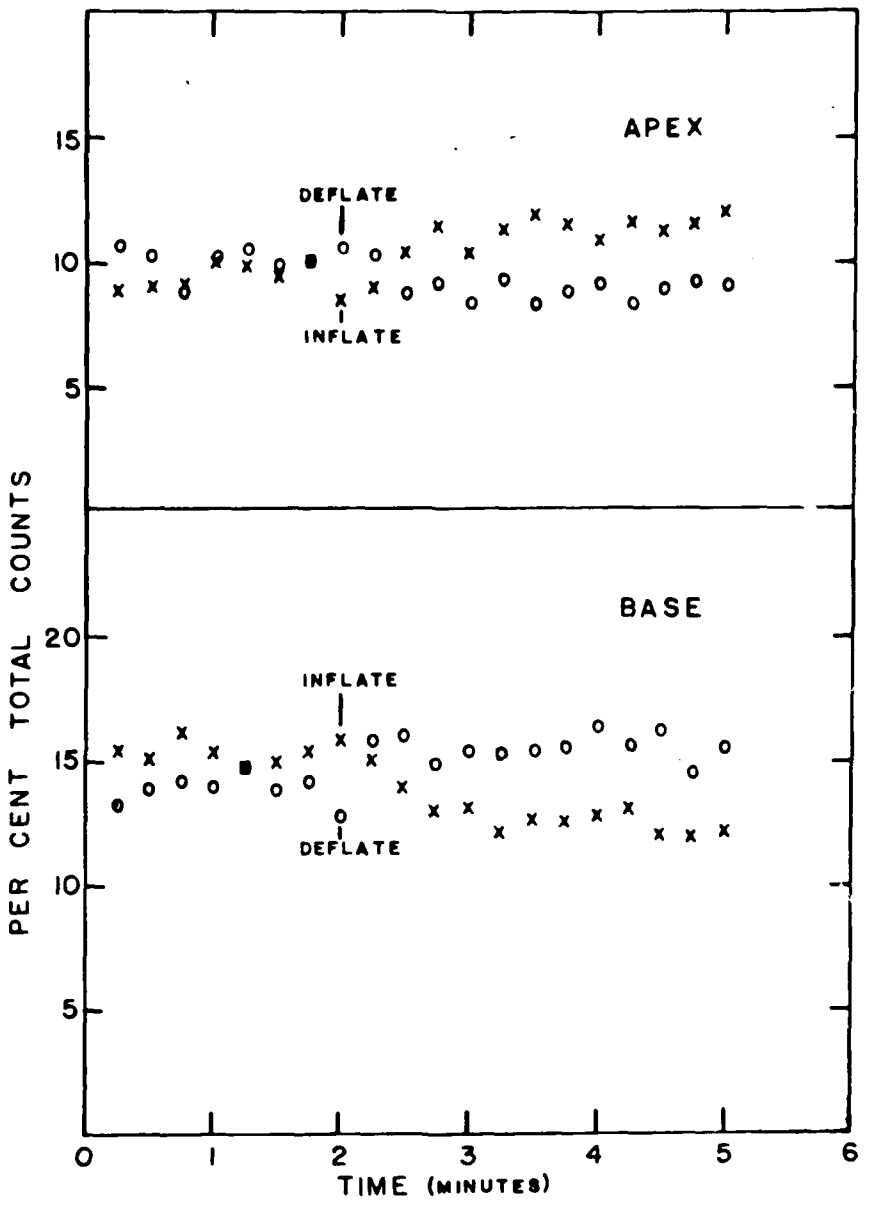

Figure I-2. Distribution of Krypton-81m near the lung apex (top panel) and base (bottom panel) during abdominal bladder inflation (X) and deflation (O) in dogs exposed to +1 Gz stress.

saturation in dogs breathing air while being exposed to +1.7 Gz. When the abdomen was not supported by counterpressure, arterial oxygen saturation fell with the onset of the G stress. However, when counterpressure was applied, arterial desaturation did not occur, in fact, it increased slightly. In the second case, the animals were vagotomized to eliminate the initial apnea seen in dogs exposed to +Gz stress (Barr et al., 1959). Minute ventilation increased with the onset of +Gz stress and bladder inflation in the vagotomized dogs which could have accounted for the increased arterial saturation. In our study, the G-stress was already present when the bladder was inflated, and no significant change in ventilation was observed (Table I-1). Therefore, saturation must have been maintained through a redistribution of ventilation and perfusion. We have been unable to find other studies in the literature in which effects of bladder inflation during air breathing have been addressed. On the basis of our data and the data of Barr et al., we would conclude that, at +1Gz, abdominal bladder inflation leads to increased ventilation in non-dependent lung regions and a more even distribution of perfusion within the lung.

II. Interaction of pulmonary mechanics and G-suit inflation during +Gz stress

The results of study I suggest that inflation of the G-suit abdominal bladder tends to enhance rather than impair gas exchange during air breathing at +1Gz. To understand the influence of the abdominal bladder on gas exchange at higher levels, it is first necessary to understand the interaction between chest wall and lung mechanics during +Gz stress and the influence of abdominal bladder inflation on that interaction. One way to examine chest wall-lung interaction is to measure regional intrapleural surface pressure (Agostoni and Mead, 1964). Although reports have appeared describing the distribution of intrapleural pressure in dogs at 0 and +1Gz (Krueger et al., 1961; Hoppin et al., 1969; McMahon et al., 1969a), none have examined the influence of high +Gz stress on this variable. Wood et al. measured intrapleural fluid pressure at various sites during +Gx stress. However, these authors did not consider the +Gz vector nor did they examine the interaction of the chest wall-lung system and the G-suit. The purpose of this study was to examine the effects of +Gz stress and abdominal bladder inflation on regional intrapleural pressure.

Methods

Nine adult male dogs weighing 21.8 $\pm$ 3.2 Kg were anesthetized with 30 mg/Kg pentobarbital sodium and intubated with a cuffed endotracheal tube. A catheter was positioned in the femoral vein for supplemental anesthesia administration, and a Millar catheter-tip pressure transducer was introduced through the femoral artery and placed in the thoracic

aorta for blood pressure monitoring. Air-filled, stainless steel cannulae were placed in two to four intercostal spaces ranging from the third to ninth intercostal space to monitor regional intrapleural pressure. The cannulae were constructed from 3 inch, 15 gauge needles. The needles were blunted and bent at a right angle 4 cm from the tip, and 24 side holes were placed along the length of the cannula. Anchors were attached to the needle hub so that the cannula could be secured with suture to the skin. The cannulae were placed in the same vertical plane in the ventral third of the rib cage, and they were directed along the intercostal space with the tips facing dorsally. Purse string sutures through the skin and at least one muscle layer were tightened around the cannulae to prevent air leakage into the intrapleural space.

After pleural pressure monitoring sites had been established, a standard G-suit abdominal bladder (CSU-12/P) was placed around the animal. The dog was placed supine on the animal end opposite the human gondola of the USAFSAM centrifuge (3.97 M radius). Imposed +Gz stress consisted of 40 second exposures (0.1 G/sec onset) to +Gz levels of +1 to +5Gz. Measurements were made with and without G-suit inflation (standard inflation scheme, 1.5 psi/G starting at +2.2Gz) using Statham P23BB pressure transducers. Between exposures, the animals' lungs were hyperinflated several times to open any atelectatic areas. All exposures were run with G-suit bladder inflation and then repeated without bladder inflation. Upon completion of the two series of exposures, the animal was sacrificed with an intravenous injection of saturated potassium chloride. The dead animal was then exposed with and without G-suit inflation to a +Gz profile consisting of 40 second steps at each +Gz level used when the animal was alive. The intent of this

portion of the protocol was to provide a means by which the effects of the exposure on the passive lung-chest wall system could be separated from any modifying influence of active chest wall muscular tone.

Results

Intrapleural pressure at each +Gz level and test condition for a given animal was determined by sampling pressure at end-expiration (FRC) at least four times during each 40 second exposure and once at each G level during the slow onset phase of the exposure. Mean data from the nine animals are summarized in Tables II-1 and II-2. Data obtained from third and fourth, fifth and sixth, and seventh and eighth intercostal spaces were pooled so that meaningful statistical analysis could be performed. Statistical analysis did not include data from the ninth intercostal space since only two experiments included cannula placement at this site.

Mean regional intrapleural pressure measured during exposure of the live animal without bladder inflation (control state) has been plotted as a function of measurement site in Figure II-1. As the +Gz stress increased, the intrapleural pressure gradient along the lung increased. Intrapleural pressure became more negative in non-dependent regions and more positive in dependent regions. No change in mean intrapleural pressure was observed at the level of the seventh and eighth intercostal space as +Gz stress increased.

The effects of muscular tone on regional intrapleural pressure are shown in Figure II-2. Intrapleural pressure at each monitoring site is plotted as a function of +Gz stress for the control state and dead dog without bladder inflation (control state minus active muscular tone).

TABLE II-1. MEAN INTRAPLEURAL PRESSURE - LIVE DOG

INTERCOSTAL SPACE	N	+Gz 0	1	2	3	4	5
				BLADDER DEFLATED			
3 - 4	7	-4.46	-7.3	-9.08	-9.59	-10.85	-12.58
	(SEM)	.58	.98	1.39	1.28	1.61	1.92
5 - 6	7	-4.37	-6.64	-7.96	-9.46	-11.4	-12.89
	(SEM)	.71	.84	1.38	1.82	2.38	2.81
7 - 8	7	-4.09	-5.47	-5.28	-5.07	-5.33	-5.12
	(SEM)	.72	1.05	1.78	2.37	3.27	4.40
9	2	-4.38	-5.7	-4.0	-2.73	+0.15	+2.05
	(SEM)	1.01	.87	1.97	2.37	3.85	3.6
				BLADDER INFLATED			
3 - 4	7	-5.27	-7.53	-9.3	-9.13	-7.18	-7.06
	(SEM)	.54	1.04	1.49	1.69	1.83	1.83
5 - 6	7	-4.99	-7.01	-8.32	-7.02	-5.86	-5.22
	(SEM)	.92	1.0	1.56	1.38	2.3	2.77
7 - 8	6	-4.3	-4.93	-3.39	+1.70	+4.74	+8.66
	(SEM)	.84	.84	1.44	2.27	3.33	4.2
9	2	-4.66	-5.83	-5.68	+0.24	+8.65	+14.87
	(SEM)	1.54	1.02	1.71	2.64	4.35	5.71

TABLE II-2. MEAN INTRAPLEURAL PRESSURE - DEAD DOG

INTERCOSTAL SPACE	N	+Gz 0	1	2	3	4	5
				BLADDER DEFLATED			
3 - 4	7	-5.1	-8.82	-11.84	-14.6	-16.51	-18.29
	(SEM)	.36	.5	.89	1.11	1.24	1.71
5 - 6	7	-4.99	-8.68	-10.44	-11.87	-12.9	-14.08
	(SEM)	.59	1.44	1.86	2.37	2.8	3.23
7 - 8	7	-5.3	-6.74	-6.72	-6.69	-6.62	-7.13
	(SEM)	.59	1.43	2.33	2.8	3.32	3.67
				BLADDER INFLATED			
3 - 4	7	-4.59	-8.65	-11.29	-7.1	-6.39	-6.26
	(SEM)	.41	.93	1.02	1.87	2.31	2.64
5 - 6	7	-4.36	-7.24	-8.13	-3.73	-2.18	-1.45
	(SEM)	.56	1.29	1.61	2.6	3.33	3.73
7 - 8	6	-5.8	-6.98	-6.25	+1.97	+5.34	+8.13
	(SEM)	.36	1.66	2.07	3.31	4.3	5.40

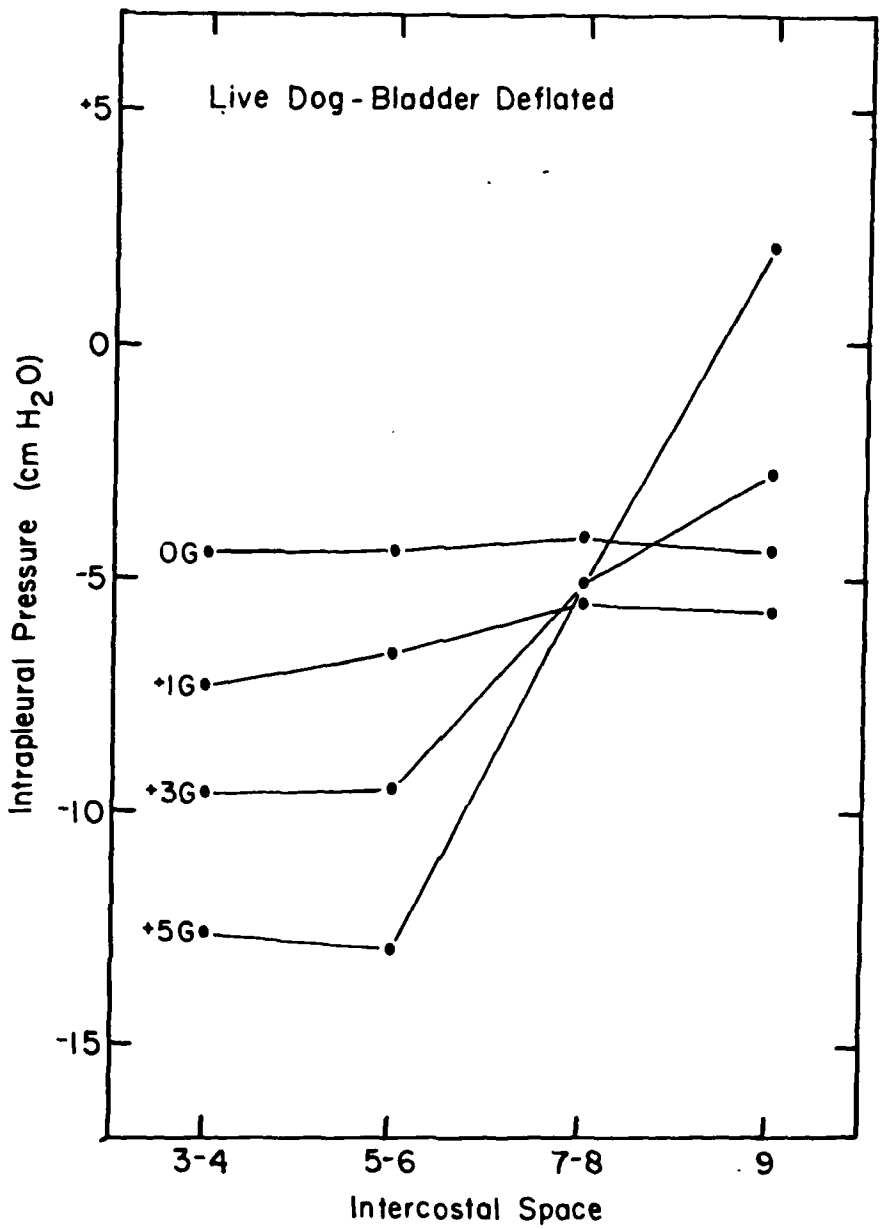

Figure II-1. Mean regional intrapleural pressue as a function of measurement site in live dogs exposed to +Gz stress without G-suit bladder inflation. Standard errors of the mean are omitted for clarity but are presented in Table II-1.

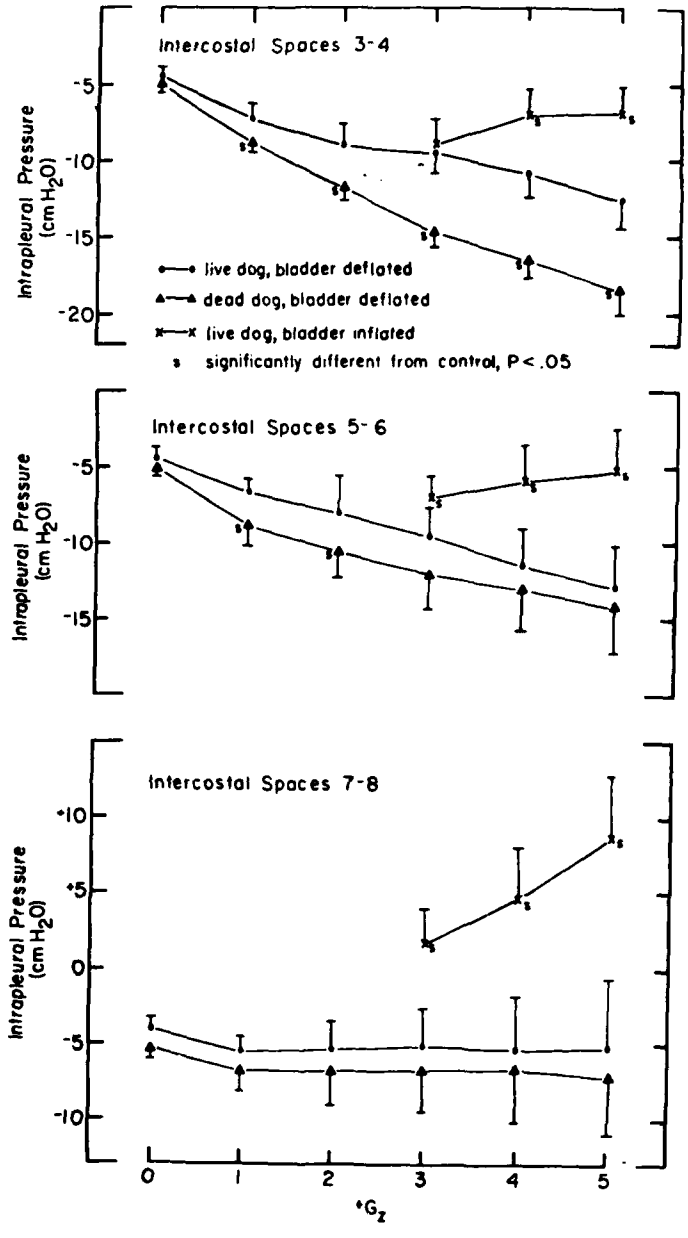

Figure II-2. Mean regional intrapleural pressure as a function of +Gz stress in live dogs without abdominal bladder inflation (•), with bladder inflation (X), and in dead dogs without bladder inflation (▲). Bladder inflation begins at +2.2 Gz and continues at a rate of 1.5 psi/G. Standard errors of the mean are indicated. Statistical significance was determined with a paired t-test.

At the level of the third-fourth intercostal space, removal of muscular tone resulted in a more negative intrapleural pressure when +Gz stress was applied. At the seventh-eighth intercostal space level, however, no significant influence of muscular tone was detected.

The influence of G-suit abdominal bladder inflation is also shown in Figure II-2. Only data obtained at +3Gz and above have been plotted since the bladder did not begin to inflate until +2.2Gz, and data obtained at the lower G levels were essentially the same as the control state. At the +3Gz level, influence of bladder inflation was detected only at the fifth-sixth and seventh-eighth intercostal space levels. In the non-dependent lung regions, intrapleural pressure approached the zero Gz level, while in the dependent regions, bladder inflation resulted in abolition of the normal negative intrapleural pressure.

Discussion

A variety of techniques have been employed to obtain direct measurements of intrapleural pressure (Wood et al., 1963; Krueger et al., 1961; Hoppin et al., 1969; McMahon et al., 1969a). McMahon et al. (1969b) used a physical model to examine the degree of error introduced by the lung distortion created when various types of measuring devices are placed between the lung and chest wall. They concluded that an air-filled needle should underestimate positive surface pressures. Because distortion is maximum when intrapleural pressure is positive, we reasoned that an indication of maximum error introduced by our cannulae could be obtained by examining how well it recorded known positive pressures in a model consisting of two pieces

of opposed skin. The model is depicted in Figure II-3. Two large pieces of dog skin with underlying fascia were moistened with saline and tacked to a piece of wood with the fascia sides opposed. A hole was made in the upper layer with a 15 guage needle, and a pleural pressure cannula was placed between the two layers of skin in the same orientation as would exist in vivo. A weighted lucite cylinder, 7.5 cm in diameter, was placed on the skin so that the cannula was within the cylinder. The air-filled cannula was connected to a Statham P23BB transducer, and water was added to the cylinder. The measured height of the water column from 0 to 35 cm H_2O was compared to the pressure measured by the cannula-transducer system. Results, shown in Figure II-4, indicated that the cannula-transducer system provided a good estimate of the applied pressure.

The magnitude of the intrapleural pressure gradient that we observed in the control state at +1Gz (Fig. II-1) is consistent with those reported by Krueger et al. (1961), Hoppin et al. (1969), and McMahon et al. (1969) in head-up, vertical dogs. At increased +Gz stress levels, the intrapleural pressure gradient increased. However, pressure at the seventh-eighth intercostal space level did not change. Bryan and his colleagues (1966) used radioactive gas techniques to assess the effect of gravity on the distribution of ventilation in man. They identified a point approximately two-thirds the lung height measured from the top of the lungs where lung volume remained constant when +Gz stress was increased to +2Gz. This finding suggests that intrapleural pressure at this point also remained constant. The seventh-eighth intercostal space in our animals corresponds to approximately the same topographical location. It is at this location

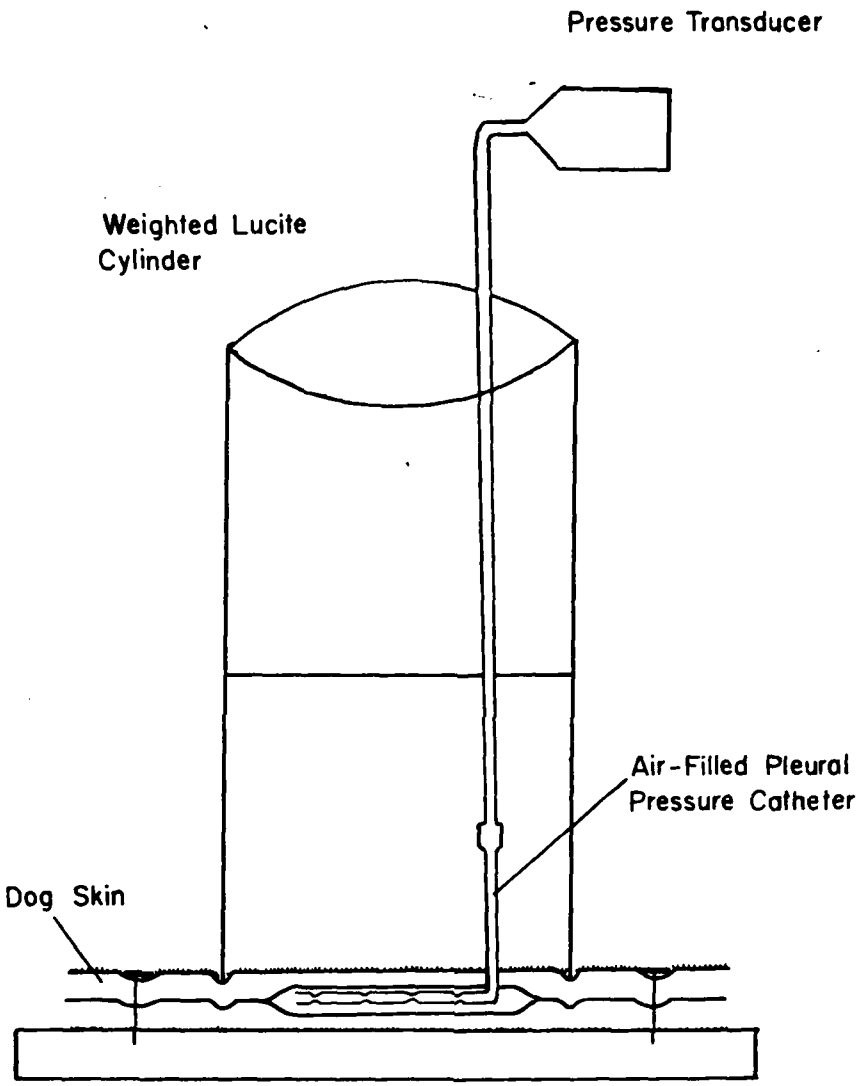

Figure II-3. Test model used for testing intrapleural pressure monitoring cannulae.

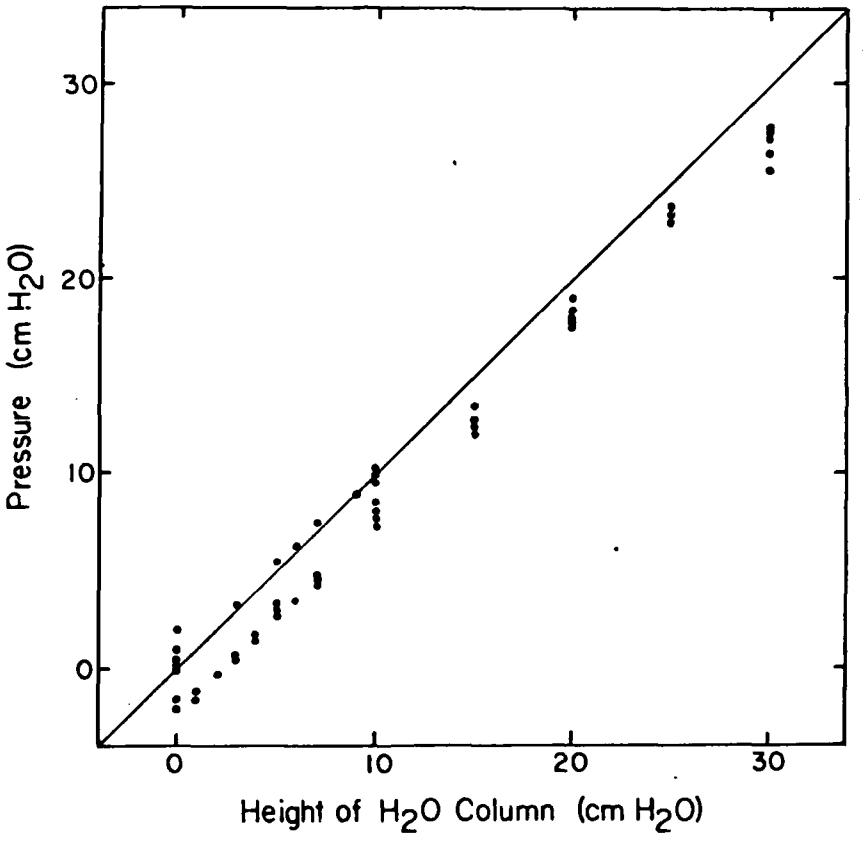

Figure II-4. Pressure measured with intrapleural pressure cannula as a function of water column height in the test model cylinder.

that the last rib attachments to the sternum occur forming a transition point for the thoracic cage. Above this point, the rib cage forms a relatively rigid container, and when +Gz stress is applied to the system, the lung is pulled away from the rib cage in a caudal direction creating a more negative intrapleural pressure (Fig. II-1). Below this point, the ribs can move more freely. Hence, when the diaphragm and abdominal contents are pulled in a caudal direction, the unattached ribs tend to be pulled inward. The net result is a smaller "container" into which the lung displaced from the upper thorax must fit, and regional intrapleural pressure becomes more positive (Fig. II-1). Glazier et al. (1967) measured alveolar size in greyhounds frozen during +Gz stress. At +1Gz, the alveoli at the apex were four times larger than at the base. At +3Gz, this ratio had increased to 11:1 supporting this hypothesis.

This hypothesis implies that if the region below the seventh-eighth intercostal space were able to accept more lung tissue, intrapleural pressure near the lung apices would become more negative with little intrapleural pressure change at the transition point. Figure II-2, where data from the live and dead animal are compared, supports this hypothesis. In the dead animal, the lack of active abdominal wall muscular tone most likely allowed further caudal excursion of the diaphragm. Intrapleural pressure at the third-fourth interspace level became more negative, but at the seventh-eighth interspace level, it did not change.

Abdominal bladder inflation altered this relationship considerably. The increased intrapleural pressure at the seventh-eighth interspace level during bladder inflation (Fig. II-2) indicates that lung

compression occurred at this level during bladder inflation. Continued bladder inflation accompanying progressively higher +Gz stress reduced the volume available to the lung tissue. Hence, regional intrapleural pressure at all levels rose.

The regional intrapleural pressures observed in this study indicate that the distribution of ventilation during +Gz stress is heavily dependent upon the degree of abdominal bladder inflation. As bladder inflation increases, progressively larger lung regions would be expected to exhibit airway closure. Without bladder inflation, more dependent lung regions would be expected to receive better ventilation. Since the detriment caused by bladder inflation is related to the amount of bladder pressure transmitted across the abdominal wall, the M-1 straining maneuver would tend to moderate the effect.

It is difficult to project from these data what effect bladder inflation has on distribution of perfusion, and, hence, on ventilation-perfusion relationships.

III. Effect of G-suit abdominal bladder inflation gas exchange during +Gz stress.

The influence of +Gz exposure on gas exchange in dogs was examined by Barr, Bjurstedt and Coleridge (1959), Glaister (1968), and Erickson, Sandler and Stone (1976). During air breathing, Barr et al. reported little change in arterial oxyhemoglobin saturation at +1.7 Gz when the abdomen was supported with counterpressure, but, when no counterpressure was provided, arterial oxyhemoglobin saturation fell.

Erickson and his colleagues (1976) saw little change in arterial oxyhemoglobin saturation in dogs exposed to +Gz levels as high as +6 Gz. These authors did not indicate that abdominal counterpressure was used.

Glaister (1968) recorded arterial oxygen tension continuously in dogs during 1-2 minute exposures to +Gz levels from +2 to +5Gz. An abdominal binder was imposed on all of Glaister's animals to limit the downward diaphragm displacement accompanying +Gz stress. Between trials, these animals were subjected to +1 Gz stress. Glaister characterized his observations as a three phase phenomenon. A progressive fall in arterial oxygen tension during +Gz exposure was followed by a transient recovery upon restoration of +1Gz. A slower recovery was then seen taking up to 1.5 minutes for complete recovery to control (+1Gz) arterial oxygen tension levels.

The counterpressure applied in the above studies differed from normal application of the G-suit abdominal bladder in that active counterpressure was not supplied as +Gz stress increased.

Although the results of Barr et al. and our study examining abdominal bladder inflation at +1Gz (Study I) suggest that abdominal restriction should help maintain arterial P_{O_2} at increased +Gz levels,

Glaister's data indicate that this does not occur.

Since his experiment did not include trials without the binder, little can be inferred concerning the relative enhancement of gas exchange afforded by the restriction.

Our pleural pressure data (Study II) indicate that continued inflation of the abdominal bladder with +Gz stress results in active lung compression suggesting that, even with air breathing, atelectasis may result with bladder inflation during +Gz stress.

This study was designed to examine the time course of gas exchange detriment resulting from +Gz stress and the influence of G-suit abdominal bladder inflation on that detriment.

Methods

Seven adult mongrel dogs weighing 19.9 $\pm$ 2.6 kg were anesthetized with 30 mg/kg pentobarbital sodium and intubated with a cuffed endotracheal tube. A Millar, catheter-tip pressure transducer was introduced through the right femoral artery and positioned in the thoracic aorta for arterial blood pressure monitoring. A 7 Fr catheter was introduced through the left femoral artery and positioned in the thoracic aorta for arterial blood sampling. A 7 Fr Swan-Ganz thermistor tip catheter was introduced through the right external jugular vein and positioned in the pulmonary artery and right atrium for thermal dilution cardiac output determinations. Because blood sampling through the distal lumen of the Swan-Ganz was not always possible at high +Gz levels, a 7 Fr side-holed catheter was also introduced through the right external jugular vein and positioned in the right ventricle for sampling mixed venous blood. Another catheter, placed in the right femoral vein, served as an injection site for supplemental anesthesia.

A standard G-suit abdominal bladder (CSU-12P) was placed around the animal, and the animal was secured to a V-board restraint in the supine position.

Four experiments were conducted on the human centrifuge at the State University of New York at Buffalo, and three animals were stressed on the animal end of the USAFSAM human centrifuge (3.97 M radius).

Remote sampling techniques were developed for expired gas collection, blood sampling and thermal dilution cardiac output determination. To allow for remote expired gas collection, the animals breathed through a Rudolph valved connected to a solenoid controlled T arrangement (Figure III-1A). In one configuration, expired gas was directed to the atmosphere, while in the second configuration, expired gas was directed into a 5 L anesthesia bag. A pressure transducer connected to the anesthesia bag allowed determination of when the bag was filled.

An air-powered piston (Figure III-1B) was used to deliver room temperature saline for thermal dilution cardiac output determinations. A 30 psi pressure source was connected to the normally closed side of a 3-way solenoid valve. One side of the solenoid was connected to the tip of a 20 cc disposable syringe. The 20 cc syringe piston and 5cc injectate syringe piston were in apposition so that when the solenoid was activated, the pressure build-up in the 20 cc syringe forced the injectate piston in, thereby injecting the bolus. A two-way solenoid valve blocked the output of the injectate syringe until the solenoid system was activated. This prevented the injectate from being drawn into the animal prematurely by the hydrostatic pressure generated by the +Gz forces.

To enable remote blood sampling, pump-syringe devices (Figure

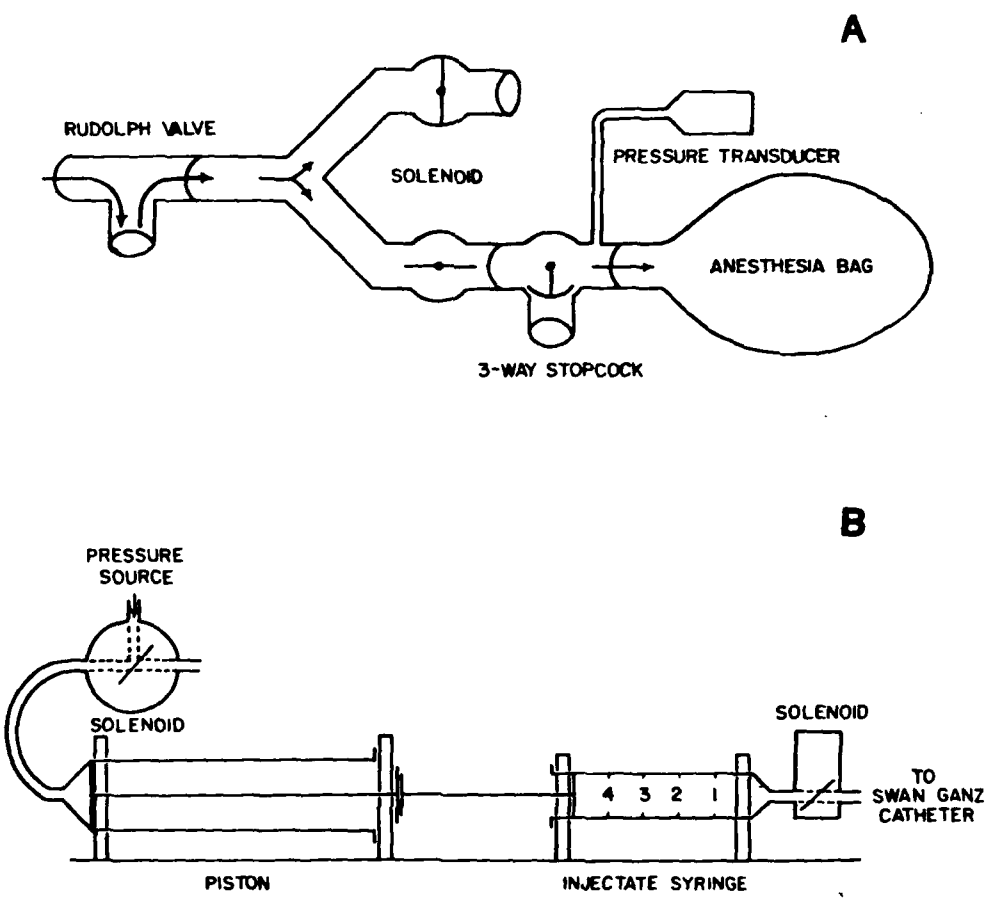

Figure III-1. A. Schematic representation of remote gas collection system.

B. Schematic representation of injector used for thermal dilution cardiac output determination.

III-2) were used that allowed collection of two samples per device. The arterial or right ventricular catheter was connected to one side of a Masterflex roller pump head. The pump outlet line passed through two miniature 3-way solenoid valves to a 20 cc syringe. Each of the 3-way valves was connected to a 10 cc sample syringe. When activated, the pump filled the 20 cc (dead space) syringe to a predetermined volume regulated by the positon of a microswitch activated by the syringe piston. The microswitch activated the three-way solenoid connected to the first sample syringe. This syringe then filled until the pump was turned off by activation of a microswitch by the sample syringe piston. When the pump was activated a second time, the process repeated for sample collection in the second sample syringe. Total dead space of the unit (with pump tubing) was less than 6cc.

Prior to the first +Gz exposure, the animal was heparinized with 3000 units of heparin sodium injected intravenously. Control samples of arterial and mixed venous blood were drawn for blood-gas analysis, a thermal dilution cardiac output determination was made, and expired gas was collected for 30 seconds. The volume of the gas sample was measured using a 1 L syringe, and it was analyzed for oxygen and carbon dioxide composition using a Perkin-Elmer MGA mass spectrometer.

Each animal was exposed to +3, 4, and 5 Gz with an onset rate of 0.1 G/sec. Exposures were made with and without G-suit abdominal bladder inflation using the standard inflation scheme (1.5 psi/G beginning at +2.2 Gz).

When the desired +Gz level was reached, expired gas collection was begun and arterial and mixed venous blood samples were drawn. The time for blood sampling was approximately 18 seconds.

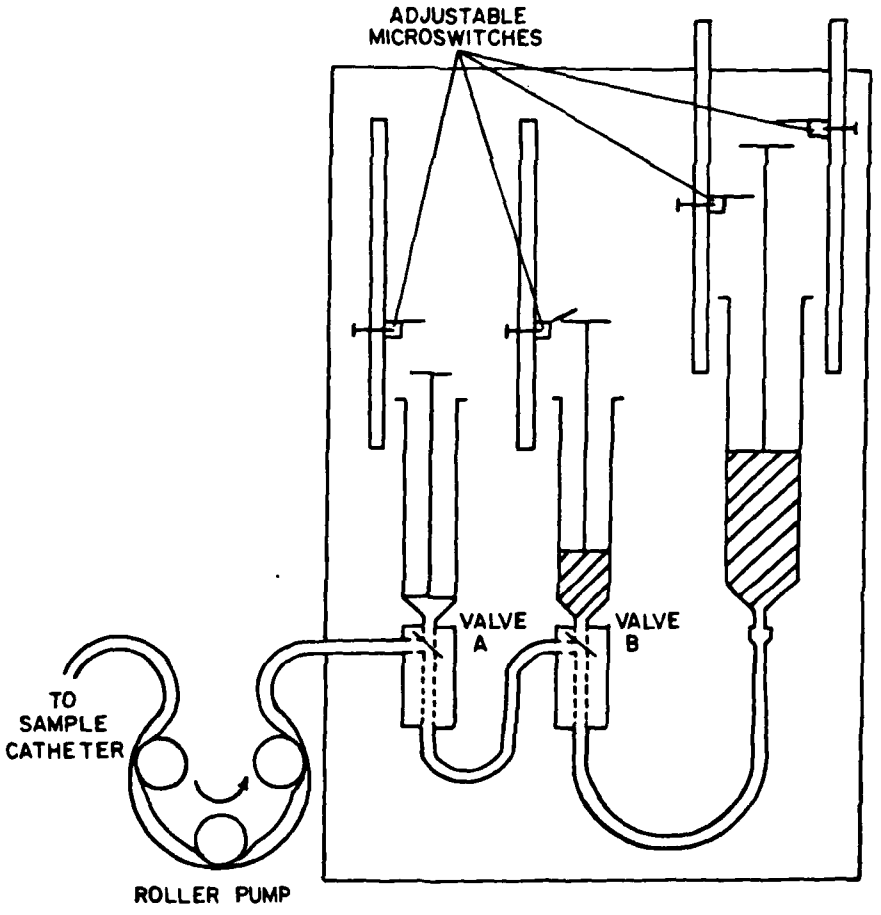

Figure III-2. Schematic representation of remote blood sampling pump-syringe device used in centrifuge studies.

Upon completion of the blood sampling, a thermal dilution cardiac output determination was made using an Edwards model 9520A cardiac output computer. The resulting curve was monitored in the centrifuge control room. At +40 seconds of the test +Gz stress, a second set of blood samples were drawn. Expired gas collection was terminated either when the bag became full as indicated by development of positive pressure in the bag or at the end of the 60 second exposure.

When 0 Gz was reached at the end of the exposure, a stopwatch was activated, the blood samples were iced for later analysis, and the expired gas was analyzed. Three minutes after reaching 0 Gz, a third set of blood samples were drawn and iced. The animal's lungs were then inflated several times with a large volume using an Ambu bag. An additional 5-15 minutes were allowed to elapse before the next exposure.

Because the SUNY at Buffalo and USAFSAM centrifuges do not have identical capabilities, +Gz exposure schemes differed slightly at the two centrifuge sites. At the SUNYAB facility, the animal was placed on a tilt table and tilted manually to +1 Gz prior to the initiation of a test run. Time at +1 Gz averaged about 35 seconds.

At the USAFSAM facility, two schemes were used. The first simulated the SUNYAB exposures. Acceleration was initiated at an onset rate of 0.1 G/sec until +1 Gz was reached. The animal was then held at that level for 35 seconds before continuing to the desired +Gz level. In the second scheme, stress was applied at 0.1 G/sec until the desired +Gz level was reached.

Although results from the two schemes differed slightly quantitatively, they were qualitatively similar. Because of this, data from both schemes were lumped with SUNYAB data for analysis.

Results

The response of arterial oxygen tension to +3, 4 and 5 Gz is shown in Figure III-3. At +3 Gz, arterial P_{O_2} did not change significantly during the exposure. This was true regardless of the G-suit abdominal bladder status.

Although the pattern was similar without abdominal bladder inflation at +4 and +5 Gz, use of the standard bladder inflation scheme resulted significant decreases in arterial P_{O_2} as the exposure continued ($P < 0.05$, Student's t-test). Furthermore, at three minutes post-exposure, the detriment was still evident. When compared to the control (0 Gz) P_{O_2}, three minutes was adequate for recovery when the G-suit was not used, but when the G-suit was used, arterial P_{O_2} remained lower than control ($P < 0.05$, Student's t-test) at this point.

Mean expired gas analysis and thermal dilution cardiac output measured at each +Gz level are summarized in Table III-1. Minute ventilation determined from gas collection during the exposure period was not significantly different from control values. Similarly, no significant differences in mixed expired gas composition were observed.

Cardiac output fell by approximately 35% during +Gz exposure without the G-suit and about 20% when the G-suit was used ($P < 0.05$, Student's t-test).

Because expired gas was collected over the majority of the +Gz exposure, data shown in Table III-1 represent a time-averaged reflection of the animal's status. The thermal dilution cardiac output values reflect status mid-exposure.

An indication of ventilation status early and late in the exposure may be obtained by examining the arterial CO_2 tension. Arterial P_{CO_2}

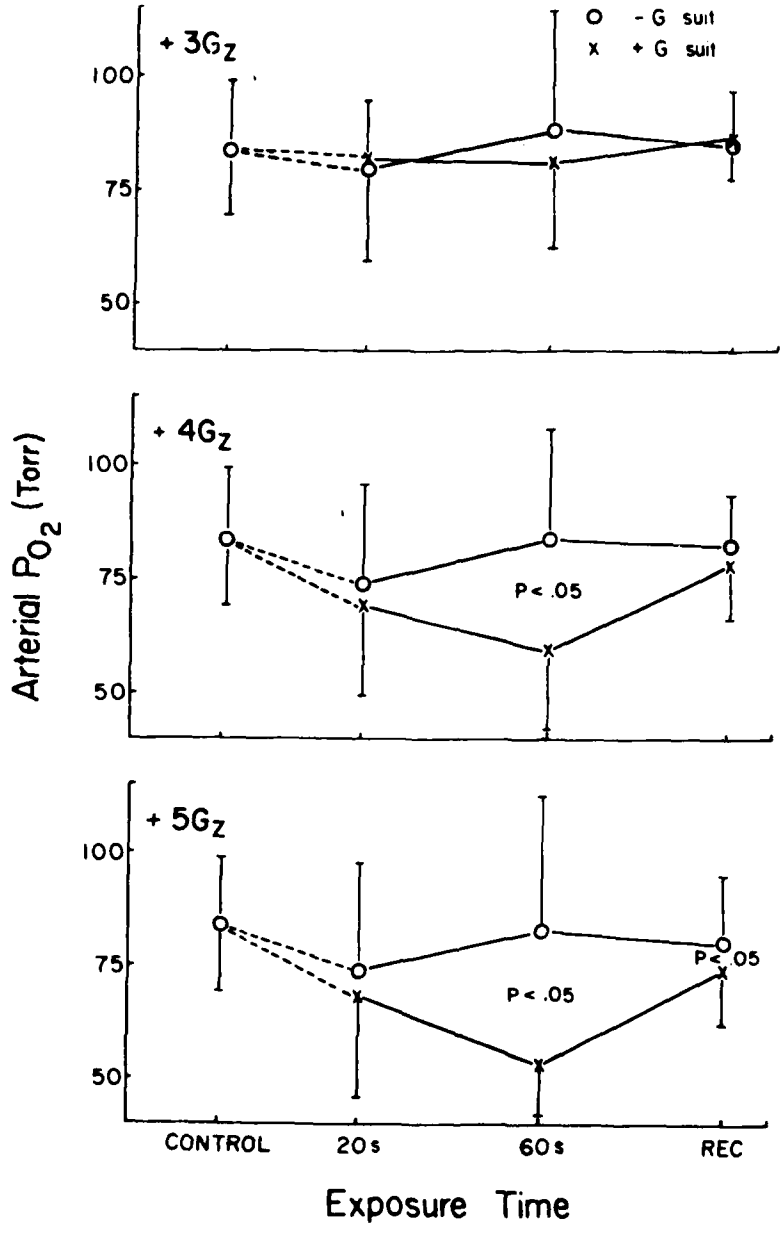

Figure III-3. Arterial oxygen tension at +3, 4 and 5 Gz as a function of sampling time without (O) and with (X) G-suit abdominal bladder inflation. Bars indicate standard deviation. Statistical significance was determined with Student's t-test.

TABLE III-1. Cardiac Output And Mixed Expired Gas Analysis

$+G_Z$		$\dot{Q}$ (L/min)	$\dot{V}_E$ (L/min BTPS)	$P_{E_{O_2}}$ (Torr)[2]	$P_{E_{CO_2}}$ (Torr)[2]	V_D/V_T X 100
0 (control)	(sd)	3.04 0.99	3.79 1.74	133 5.1	21.4 4.9	44.8 12.1
				WITHOUT G-SUIT		
3		-	-	135.5	18.8	-
	(sd)			10.4	4.1	
4		1.96 *	4.95	140.2 *	20	43
	(sd)	0.67	1.87	7.7	2.1	10.7
5		1.93 *	4.67	139.7 *	18.1	46
	(sd)	0.93	2.36	7.3	3.9	8.09
				WITH G-SUIT		
3		-	-	129.8	22.8	-
	(sd)			4.6	2.5	
4		2.47	3.87	138 *	18.8	49.1
	(sd)	1.54	1.46	6.4	2.5	15.0
5		2.40 *	3.74	140.1 *	18.4	49.0
	(sd)	1.19	2.3	11.2	3.6	14.5

* significantly different from 0 G_Z ($P<0.05$, Student's t-test)

data are shown in Figure III-4. At +4 Gz, Pa_{CO_2} remained essentially constant during the exposure regardless of the G-suit status. After the exposure, however, Pa_{CO_2} rose ($P<.01$, Student's t-test) indicating that the alveolar ventilation decreased relative to the rate of CO_2 arrival to the alveoli.

At +5 Gz the pattern seen when the G-suit abdominal bladder was used was similar to the +4 Gz exposure. When the bladder was not inflated, the animal's alveolar ventilation increased relative to CO_2 arrival at the lung as the +Gz stress continued. This is indicated by the decreasing Pa_{CO_2} seen during the exposure (Fig. III-4).

Assuming that CO_2 production remained relatively constant during the +Gz stress, an indication of cardiac output changes during the exposure may be obtained by examining the mixed venous-arterial CO_2 content differences:

$$\dot{Q} = \dot{V}_{CO_2} / (C\bar{v}_{CO_2} - Ca_{CO_2})$$

Mixed venous-arterial CO_2 content differences calculated from analysis of blood sampled before, during and after +4 and +5 Gz stress are shown in Figure III-5. Carbon dioxide contents were calculated from blood gas tensions using the computer routines of Olszowka and Farhi (1968). Carbon dioxide was used instead of oxygen because hemoglobin was estimated from the hematocrit in some experiments, and CO_2 content is less sensitive to small errors in hemoglobin determination than is oxygen content.

Figure III-5 suggests that G-suit bladder inflation helped restore cardiac output even at +5 Gz. The progressive increase in mixed venous-arterial CO_2 content difference when the abdominal bladder was not inflated indicates a progressive fall in cardiac output during the

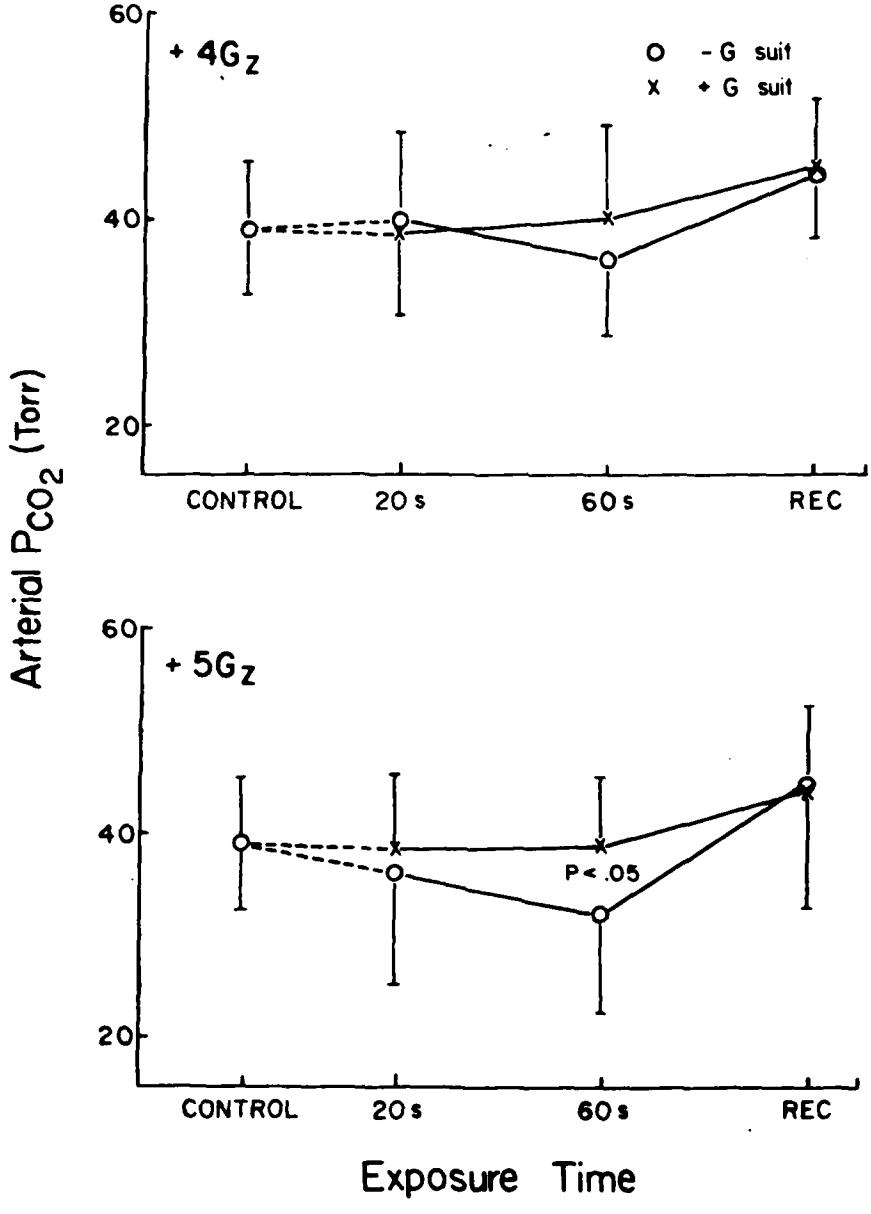

Figure III-4. Arterial carbon dioxide tension at +4 and 5 G as a function of sampling time without (O) and with (X) G-suit abdominal bladder inflation. Standard deviations are indicated. Statistical significance was determined with Student's t-test.

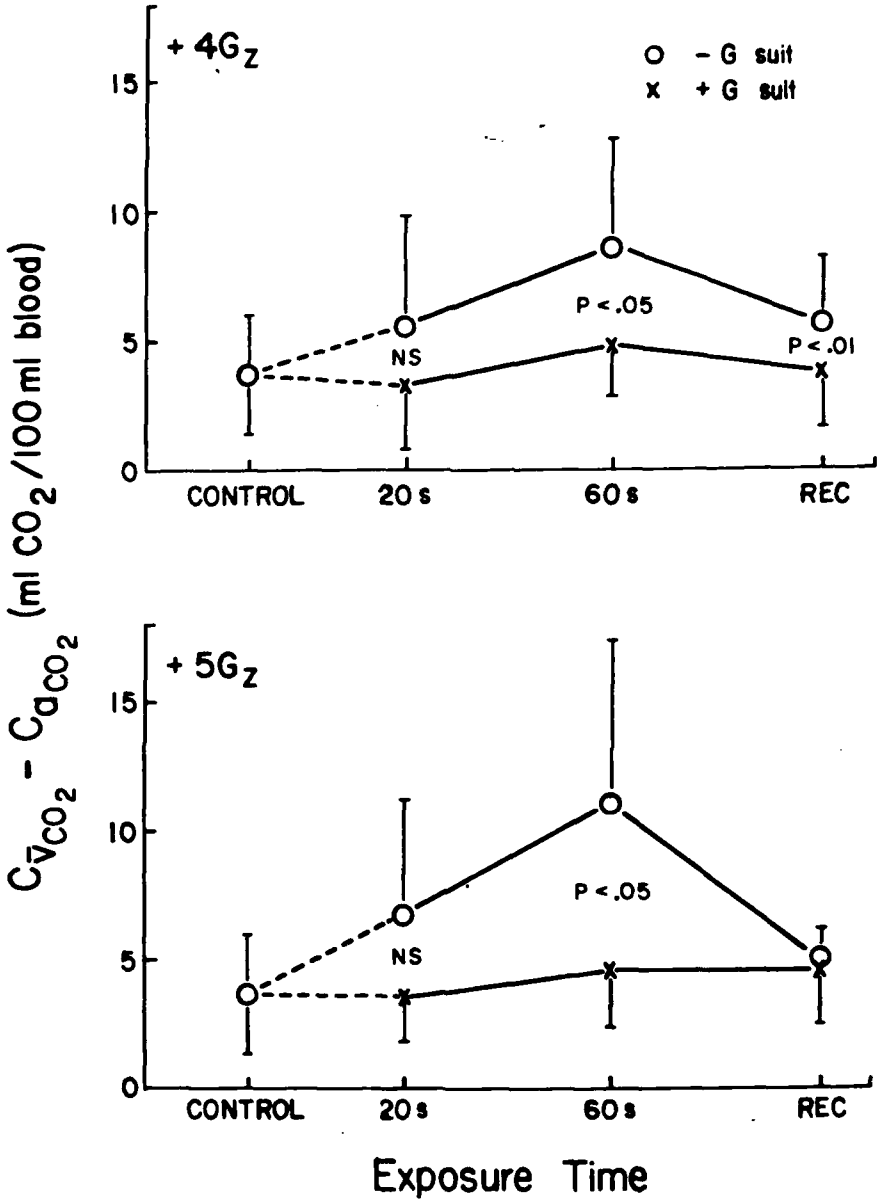

Figure III-5. Calculated mixed venous-arterial blood carbon dioxide content as a function of sampling time without (O) and with (X) G-suit abdominal bladder inflation. Contents were calculated from blood gas values using computer routines based on those of Olszowka and Farhi (1968). Standard deviations are indicated. Statistical significance was determined with Student's t-test.

+Gz stress. Further, in the case of the +4 Gz stress, more than three minutes were required for cardiac output recovery to control values ($P<.025$, Student's t-test).

Discussion

Because of technical considerations, we assumed in this study that right ventricular blood provided an adequate reflection of mixed venous blood gas status. To test this assumption, we compared the blood gas status of blood sampled from the pulmonary artery and right ventricle of two anesthetized, spontaneously breathing dogs.

Results are shown in Figure III-6. The mean oxygen tension of twenty right ventricular samples was 35.5 ± 1.52 Torr while pulmonary arterial samples drawn at the same time had a mean P_{O_2} of 36.3 ± 1.02 Torr ($P<0.01$, Student's t-test). No significant differences were detected in the carbon dioxide tensions of blood sampled from the two sites.

Although the mean P_{O_2} of pulmonary artery blood was found to be statistically higher than right ventricular blood, the magnitude of the error was about 2 to 3%, comparable to the error expected from multiple determinations on one sample. We feel that, for the purposes of this study, right ventricular blood provided an adequate estimate of mixed venous blood gas status.

The drop in cardiac output accompanying +Gz stress in this study (Table III-1) is comparable to that reported by other investigators (Glaister, 1970b; Hershgold and Steiner, 1960; Peterson, Bishop and Erickson, 1977). Data presented in Table III-1 suggest that application of the G-suit abdominal bladder tended to restore cardiac output toward the control value. This is consistent with Study I results.

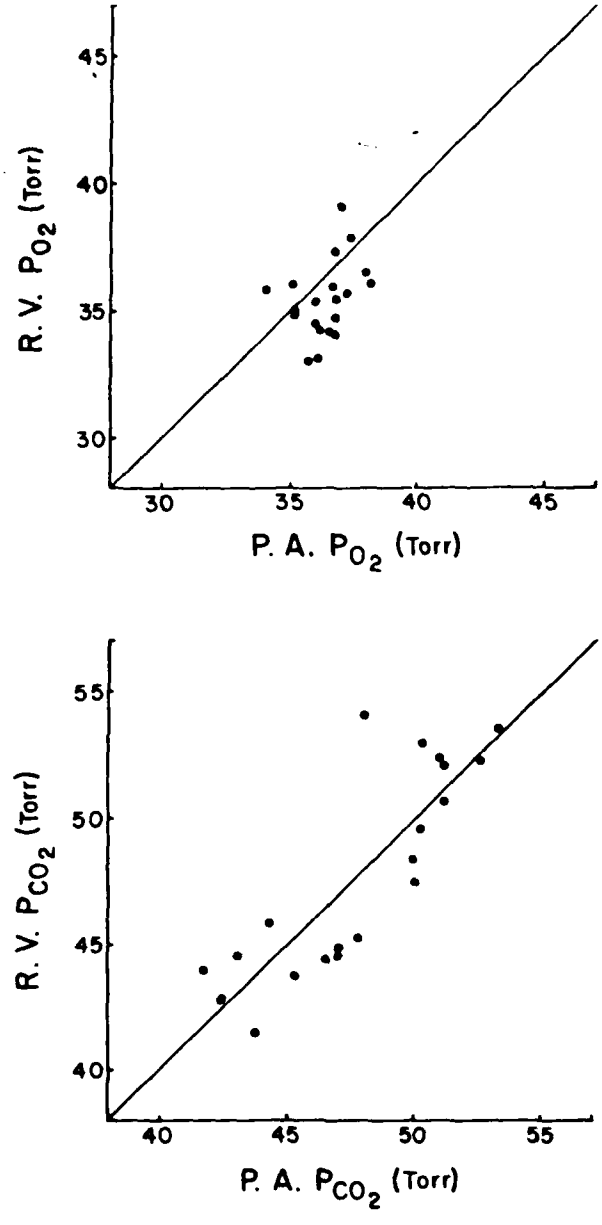

Figure III-6. Comparison of oxygen (top panel) and carbon dioxide (bottom panel) tensions measured from 20 samples (2 dogs) drawn from right ventricle with those from 20 samples drawn from the pulmonary artery.

Figure III-5 provides an indication of the time course of cardiac output changes when +Gz stress was applied. Early in the exposure, abdominal bladder inflation did not enhance cardiac output. However, as the exposure continued, cardiac output in trials without the G-suit became compromised to a greater extent. An additional 36% detriment occurred at +4 Gz and, at +5 Gz, an additional 39% detriment was overcome by use of the abdominal bladder.

Although the G-suit tended to maintain cardiac output, a continued fall in arterial P_{O_2} accompanied its use at the higher +Gz levels (Fig. III-3). A 25-30 Torr P_{O_2} detriment was evident as the exposure continued suggesting that a larger maldistribution of ventilation-perfusion relationships was present when the G-suit was used.

Arterial CO_2 tension data (Fig. III-4) indicates that alveolar ventilation relative to CO_2 arrival at the lung increased as the exposure continued without bladder inflation. These results are compatible with several interpretations.

One interpretation is that the changes in blood gases reflect ventilation-perfusion maldistribution changes resulting solely from the cardiac output differences.

As cardiac output falls, less CO_2 is returned to the lung. Thus arterial P_{CO_2} would also fall despite no change in alveolar ventilation. Any change in arterial P_{O_2} by this mechanism would reflect the degree to which mixed venous blood mixed with arterial blood through low $\dot{V}_A/\dot{Q}$ areas and intrapulmonary shunt. If the degree of venous admixture remained constant or increased as cardiac output fell, arterial P_{O_2} would be expected to drop. This did not occur without G-suit inflation (Fig. III-3). By this mechanism, one would conclude that a better

distribution of ventilation-perfusion relationships resulted from the fall in cardiac output. In a OG environment, this is indeed possible. However, it has been well established that increased +Gz stress results in a greater distribution of blood flow to dependent lung regions (Bryan et al., 1965; Glaister,1970b; Whinnery et al., 1979). Furthermore, the minute ventilations measured without the G-suit tended to be higher than those measured with the suit (Table III-1). Although this difference was not found to be statistically significant, the mixed expired gas and blood gas analyses are consistent with an increased ventilation.

A second interpretation of the blood gas data is that major changes in ventilation-perfusion maldistribution were associated with abdominal bladder inflation. Results of Study I at +1 Gz and data presented by Barr et al. (1959) at +1.7 Gz predict that maintenance of cardiac output through G-suit usage should improve the ventilation-perfusion distribution compared to no bladder inflation. We concluded, on the basis of blood gas values and Krypton-81m images of ventilation distribution that, at +1 Gz, bladder inflation promoted a better perfusion distribution to the non-dependent lung regions (see Study I). Barr et al. showed a slight increase in arterial P_{O_2} at +1.7 Gz in animals with an abdominal binder.

At higher +Gz levels, this does not appear to be the case. The continued decrease in arterial Po2 (Fig. III-3) seen with abdominal bladder inflation indicates a greater distribution of blood flow to low $\dot{V}_A/\dot{Q}$ areas. This could reflect an increase in blood flow to all areas resulting from the relatively higher cardiac output. If this were the case, a greater percentage of the increased flow would be expected to be distributed to dependent lung regions thereby causing a greater

shunt-like effect from areas whose ventilation-perfusion ratios are already low.

The intrapleural pressure measurements from Study II indicate that G-suit bladder inflation causes positive intrapleural pressures over a significant portion of lung. These pressures are of sufficient magnitude to cause lung compression. Hence, as +Gz stress is imposed with G-suit abdominal bladder inflation, the action of the bladder may promote airway closure in a larger lung region than similar exposures without abdominal bladder usage. The increase in airway closure would lead to low $\dot{V}_A/\dot{Q}$ and atelectatic areas which would be reflected by a significantly lower arterial P_{O_2} (Fig. III-3).

Glazier and his colleagues (1967,1968) examined alveolar size in dogs frozen intact while exposed to several levels of +Gz stress. At +3 Gz without an abdominal binder, a smaller alveolar volume than the +1 Gz control lung was encountered only at levels 25 cm below the lung apex. With an abdominal binder, alveoli at 10-15 cm below the apex were significantly smaller than the +1 Gz control. At the 25 cm level, alveoli were 8-9% of the volume of apical alveoli with the binder compared to 27% of the apical alveolar volume at +3 Gz without the binder.

Glaister (1968) examined the lungs of a dog exposed to +1 Gz for 4.75 hr and to six one-minute exposures of up to +4 Gz. An abdominal binder was used, and the animal breathed air throughout. Glaister described the appearance of most alveoli in sections taken from the lung base as "closed off vacuoles in an otherwise solid tissue."

The abdominal binder used by Glazier et al. and Glaister did not produce increasing active counterpressure or abdominal compression as

does the G-suit abdominal bladder. Hence, any airway closure and atelectasis seen with abdominal binders would be expected to be exacerbated by use of a continually inflating abdominal bladder.

The fact that arterial P_{O_2} did not return to control values after +4 Gz and +5 Gz exposure with the G-suit ($P<.05$, Student's t-test) but did return after similar exposures without the suit (Fig. III-3) suggests that atelectasis developed as a result of the bladder inflation. Furthermore, three minutes was not sufficient time for the animal to reopen these areas.

The implication of these findings is that the detriment associated with abdominal bladder inflation would be cumulative during repeated +Gz exposures. Arterial oxyhemoglobin saturations monitored during repeated +4 to +4.5 Gz exposures in men breathing air and using a G-suit supports this hypothesis (Barr, 1962).

It has been generally agreed that acceleration atelectasis occurs only when the +Gz stress is accompanied by 100% oxygen breathing and use of a G-suit. The results of this study and data of Michaelson and his associates (Burton, Leverett and Michaelson, 1974) indicate that exposure to high levels of +Gz stress with G-suit inflation is sufficient to cause atelectasis even though the subject breathes air. Our results further indicate that this detriment results from the increased intrapleural pressures that accompany G-suit abdominal bladder inflation.

IV. Use of Krypton-81m to examine continuous distribution of ventilation

When a radioactive tracer is present in inspired gas, its concentration within the lung is a function of the rate at which it is delivered, the rate at which it is removed by ventilation, and the rate at which the isotope decays. If the isotope has a half-life which is long relative to the ventilation removal rate (e.g. Xenon-133, half-life = 5.3 days), a steady state is reached in which the concentration in poorly ventilated areas becomes equal to that in well-ventilated areas. When this state is reached, activity over the lung reflects the distribution of volume rather than ventilation. If the isotope's half-life is short relative to the ventilation removal rate (e.g. Krypton-81m, half-life = 13 seconds), a steady state is not reached. Hence, the activity over the lung should reflect distribution of ventilation rather than volume (Goris et al., 1977). Figure IV-1 shows this relationship for a one compartment model of the system (Jones, 1978). It has been assumed that the one compartment model can be extended to the lung. However, this assumption has not been tested in an animal preparation. The purpose of this study was to examine the relationship between ventilation and Krypton-81m activity measured over the lung during continuous Krypton-81m inhalation. Variables considered included acquisition mode, acquisition view, tidal volume and frequency changes, end-expiratory volume, and the inspiratory to expiratory time ratio.

Methods

Sixteen adult mongrel dogs weighing 19.1 $\pm$ 1.9 Kg were used in this

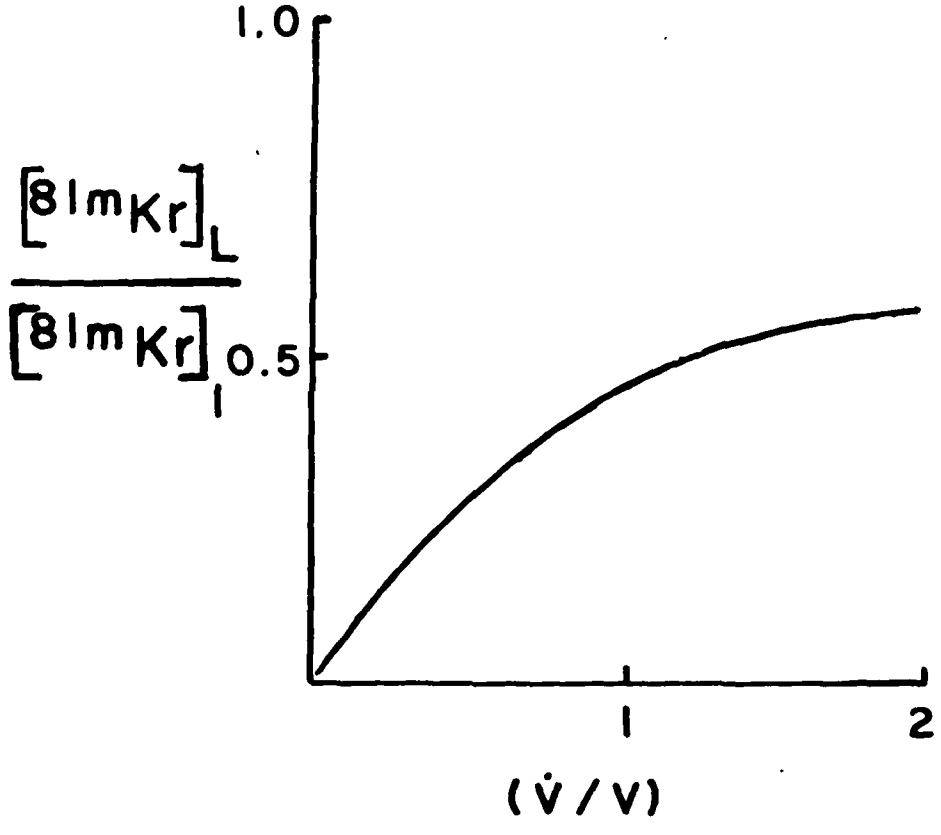

Figure IV-1. Theoretical prediction of Krypton-81m concentration as a function of ventilation per unit lung volume in a well mixed, one compartment model.

study. The animals were anesthetized with 30 mg/Kg pentobarbital sodium and intubated with a cuffed endotracheal tube. Catheters were placed in the jugular vein and carotid artery for supplemental anesthesia administration and systemic arterial blood pressure monitoring. All animals were paralyzed with 5 mg/Kg succinylcholine (Anectine) administered intramuscularly and ventilated with a Harvard Apparatus Model 613 ventilator. Gas to the ventilator was supplied from a reservoir bag in which air was mixed continuously with Krypton-81m. The Krypton was obtained by passing air through a generator consisting of Rubidium-81m fixed to an ion exchange column. As the Rubidium-81m decays to Krypton-81m, the Krypton is eluted by the gas flow. Generators were made on-site using the University of Washington Nuclear Physics facility or obtained commercially.

Four types of experiments were conducted. Effects of ventilation on count rate using two acquisition modes were determined by changing frequency at a constant tidal volume in eight animals and by changing tidal volume at a constant frequency in four animals. In another three animals, ventilation was fixed, and the time of inspiration was varied from 30 to 70 per cent of the respiratory cycle. Data were acquired either as "static" or "gated" images from an anterior view of the supine animal. In the static mode, activity over the lung was recorded for 100-120 seconds as one image. In the gated mode, the camera and computer were triggered to begin acquiring images at a given point during the respiratory cycle. Twenty-eight images were acquired per breath. The scheme was repeated on successive breaths with the images from one breath added to the accumulated images from the previous breaths. Acquisition continued until 40 thousand counts per frame were

acquired. In each experiment, a ventilation level was set, and several minutes were allowed for a steady state to be established. The static image was acquired, and, after several minutes, the gated study was acquired. A new experimental condition was then established, and the process was repeated.

Influence of end-expiratory volume on count rate was determined in four animals. These animals were ventilated at different rates with positive end-expiratory pressures (PEEP) of 0, 5 and 10 cm H_2O imposed. Data were acquired from an anterior view using the gated technique. Functional Residual Capacity (FRC) was measured using an indicator dilution technique. The animal was removed from the ventilator and ventilated with a 1 liter syringe containing a known quantity of Xenon-133. Xenon activity in the syringe was again determined after 20 breaths of rebreathing (approximately 400 cc per breath), and FRC was calculated using standard indicator dilution equations. To determine the change in volume from FRC at each PEEP level, the animal was disconnected from the ventilator, and its lungs were inflated to the previous peak inspiratory pressure with a 1 liter syringe. Volume was then withdrawn until the appropriate PEEP level was attained. The difference between the starting volume (airway pressure =0) and the PEEP level was assumed to equal the change in lung volume from FRC at end-expiration.

The purpose of the fourth set of experiments was to determine if acquisition view affects the quantitative nature of the image obtained. In five animals, a series of gated images were obtained at several ventilation rates and PEEP levels using an anterior view of the supine animal. FRC was determined with Xenon-133, and the sequence was repeated while gated images were obtained using a posterior view.

Results

Data from the static studies relating Krypton activity over the lung to ventilation are shown in Figure IV-2. Activity has been corrected for background and normalized to the activity of the inspired gas. The end-expiratory volume to which ventilation was normalized was estimated on the basis of body weight (Stahl, 1967) or measured directly as indicated above. Figure IV-2 demonstrates that activity is related to ventilation in a nearly linear fashion and that this relationship is independent of the tidal volume-frequency combination used to acheive a given ventilation.

Experimental data are compared to the theoretical prediction of concentration as a function of ventilation in Figure IV-3. Because lung volume varies between FRC and end-inspiratory volume during a static acquisition, it is difficult to determine what volume is most appropriate when calculating Krypton concentration within the lung. Hence concentration was calculated at FRC and at end-inspiratory volume. The true concentration at any level of ventilation should lie between these extremes. It appears from Figure IV-3 that Krypton-81m concentration is more linearly related to the normalized ventilation than theory predicts. Data analyzed in a similar manner from the gated studies yielded similar results. This relationship was not altered by varying the time allowed for inspiration from 30 to 70 per cent of the respiratory cycle.

We postulated that the discrepancy between theory and the experimental data could be explained if the effective volume being ventilated changed with ventilation. To test this hypothesis, we analyzed data from images acquired using the gated acquistion mode.

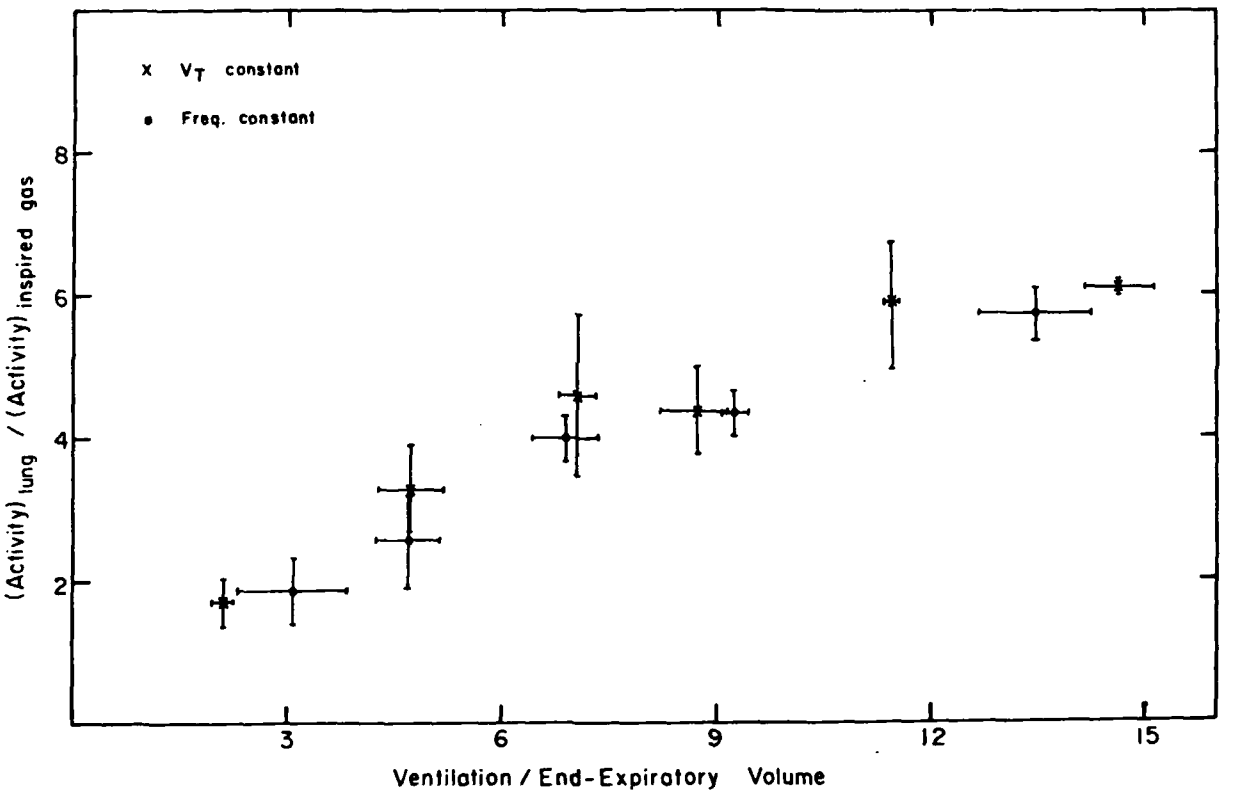

Figure IV-2. Krypton-81m activity measured over the lung as a function of ventilation/volume. Ventilation was changed by changing frequency at a fixed tidal volume (X) or by changing tdial volume at a fixed frequency (•). Standard errors of the mean are indicated.

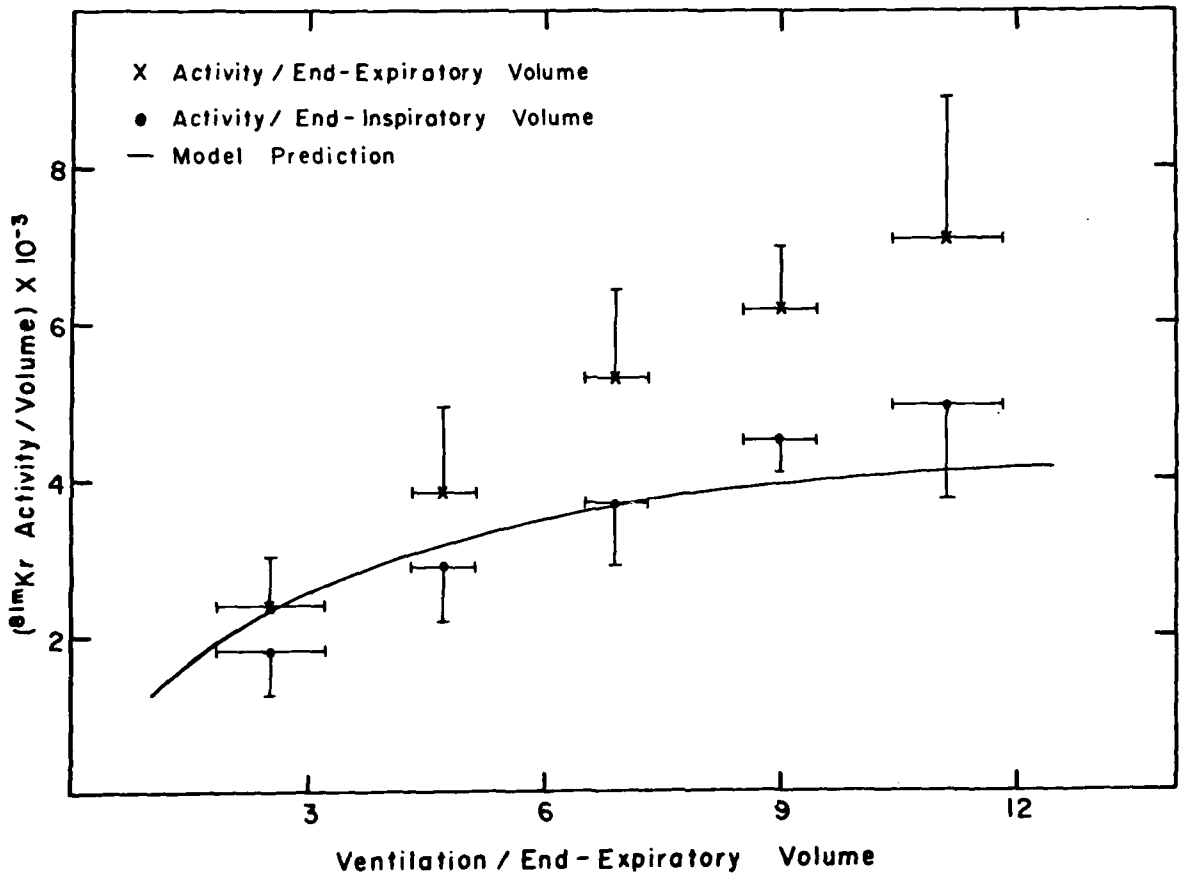

Figure IV-3. Krypton-81m concentration measured over the lung as a function of ventilation/volume compared to a well mixed, one compartment model prediction. Concentration was calculated assuming volume remained constant at either end-expiratory (X) or end-inspiratory (•) volume. True concentration at any ventilation level should lie between these extremes. Standard errors of the mean are indicated.

A typical plot of activity over the lung as a function of time during the respiratory cycle obtained from a gated study in one animal experiment is shown in Figure IV-4. We reasoned that the peak activity seen during the cycle should be proportional to the total lung volume to which the Krypton-81m is distributed at end-inspiration (V_1). Similarly, the minimum activity, corrected for Krypton-81m decay, should be proportional to the Krypton-81m distribution volume at end-expiration (Vo). If these relationships are true and if tidal volume is known, the end-expiratory volume can be calculated from the gated study activity curve as follows.

$$Apeak / Amin = V_1 / Vo = (Vo+Vt)/Vo$$

where Apeak = peak activity

Amin = minimum activity corrected for Krypton-81m decay

Vt = tidal volume

Rearranging terms:

$$Vo = (Vt\ Amin) / (Apeak - Amin)$$

To test this method of analysis, we repeated a typical experiment using a three liter weather balloon instead of the dog. The bag was arranged so that it had a constant "end-expiratory" volume of 900 ml. Ventilation was changed by changing frequency at a constant tidal volume and by changing tidal volume at a constant frequency. Krypton-81m activity over the bag was assessed using the gated mode for data acquisition.

End-expiratory volume was calculated in this manner for the bag studies and for the dog studies in which end-expiratory volume was

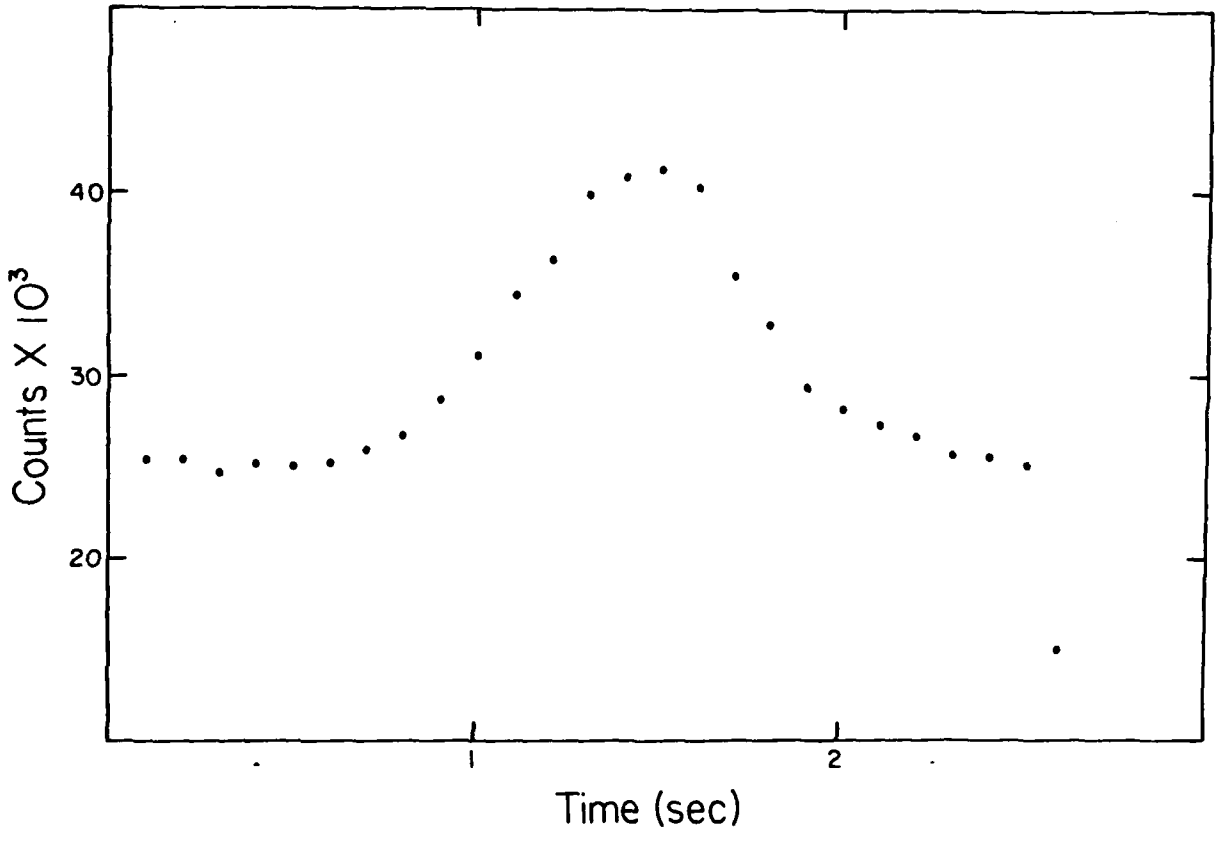

Figure IV-4. Krypton-81m activity measured over the lung for the respiratory cycle. Data obtained from a gated study (see text). The last point "drops out" indicating completion of the respiratory cycle within 25 frames.

measured independently. The calculated values were then compared to the measured values. Results are shown in Figure IV-5. In the bag study, the calculated end-expiratory volume provided a good estimate of the measured value. However, in the dog studies, the calculated value consistently underestimated the measured end-expiratory volume. The degree to which the calculated value underestimated the measured value was independent of acquisition view but depended upon ventilation. Furthermore, the extent to which ventilation affected the FRC estimate depended upon how the ventilation change was achieved. This is illustrated in Figure IV-6 where representative data from three animals are presented. The FRC estimate obtained from ventilation increases resulting from tidal volume increases were significantly higher ($P<.025$, unpaired t-test) than those obtained at comparable ventilations achieved by increasing respiratory frequency. These data suggest that the distribution volume of Krypton-81m in the lung is substantially less than the end-expiratory volume and is dependent upon a number of variables.

Discussion

The discrepancy between volume calculated from Krypton-81m data and that measured with Xenon-133 could reflect the degree to which the Krypton-81m mixes with resident gas or experimental error in the Xenon-133 dilution technique used to measure end-expiratory volume. The latter is unlikely since "end-expiratory" volume measured repeatedly with Xenon-133 in the bag study was consistently within 5 per cent of that measured with a 1-liter syringe, and, in the dog, the relatively long half-life Xenon-133 would be expected to be well distributed within

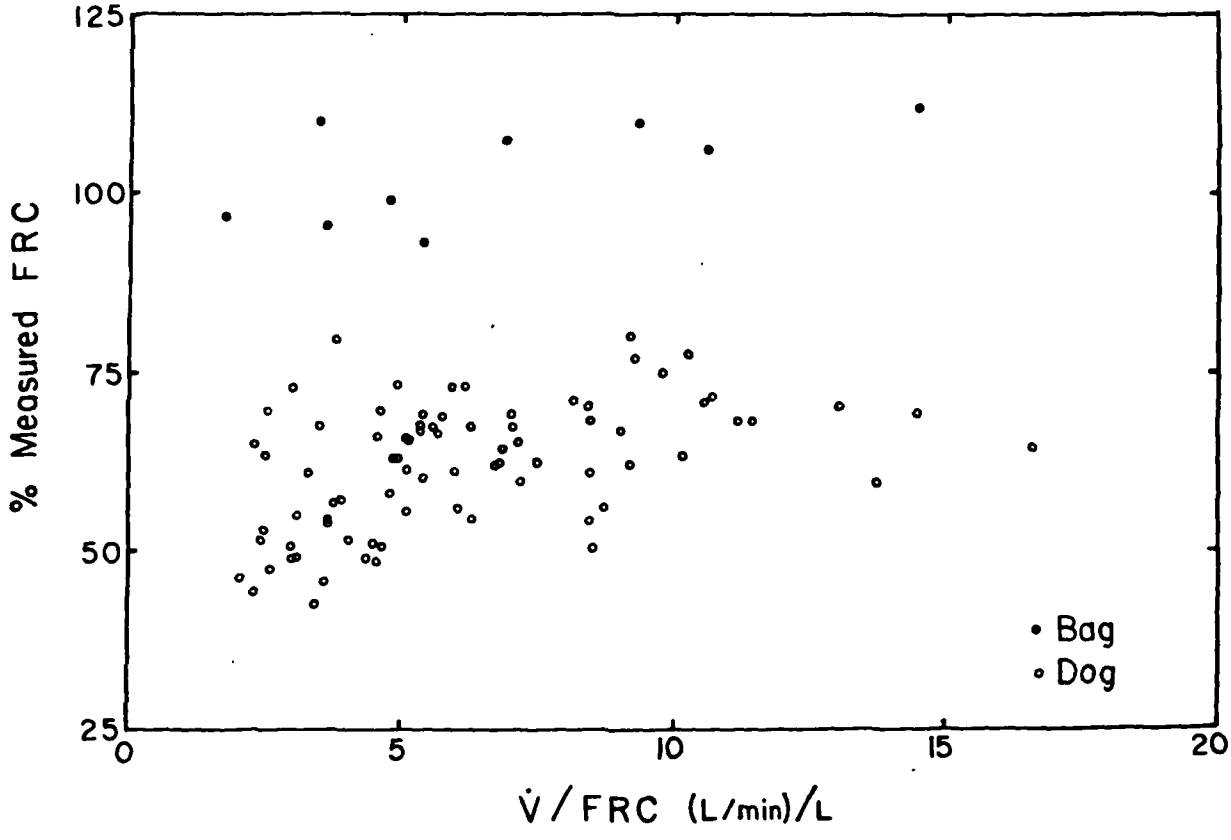

Figure IV-5. End-expiratory volume calculated from gated studies as a function of ventilation/volume. Calculated values are expressed as per cent of the measured end-expiratory volume. Data from ventilated bag study (●) and dog studies (○) are shown.

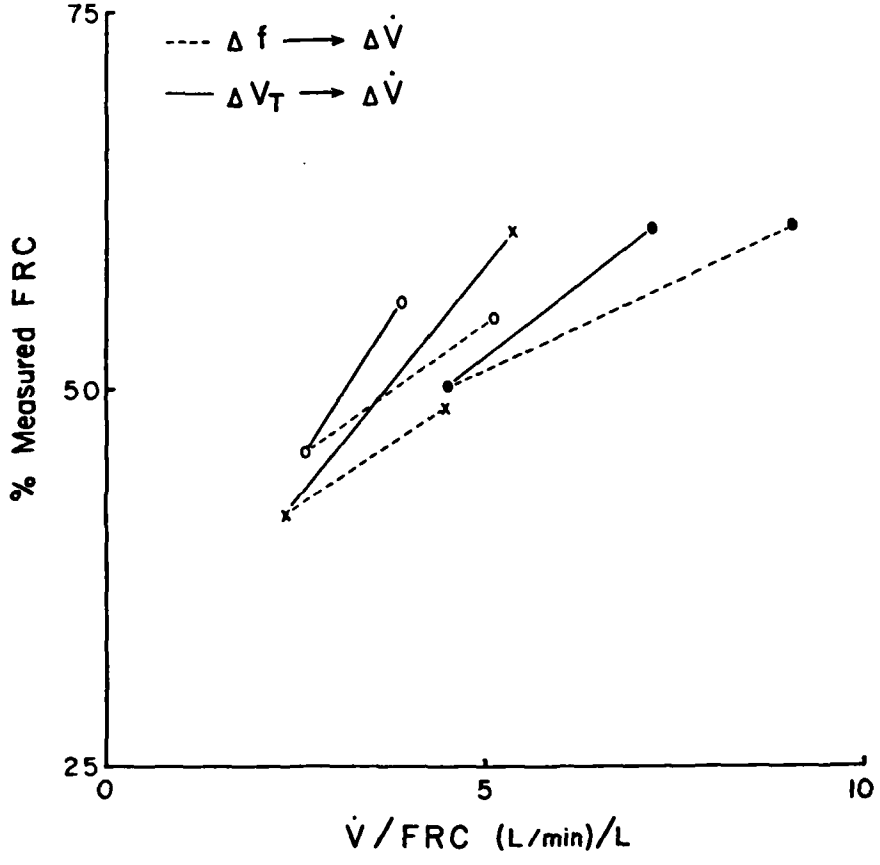

Figure IV-6. End-expiratory volume calculated from gated studies as a function of ventilation/volume in 3 dogs. Calculated values are expressed as per cent of the measured end-expiratory volume. Ventilation was increased by increasing frequency at a constant tidal volume (dashed line) or by increasing tidal volume at a constant frequency (solid line).

the lung volume after twenty breaths of rebreathing.

The more likely explanation is that the underlying assumption upon which our analysis is based, that is, Krypton-81m is well mixed with the resident lung gas during inspiration, is not valid. Failure of Krypton-81m to mix well during inspiration would result in gas relatively rich in tracer leaving the system during expiration. The gas remaining would have disproportionately less tracer, and an underestimate of the true volume would be obtained from the analysis.

On the basis of this hypothesis, a larger resident volume would be calculated if conditions were altered to favor gas mixing. In the three animals in which inspiration time was varied at a fixed tidal volume and frequency, the end-expiratory volume calculated from the gated acquisitions increased from a mean of 549 $\pm$ 16.1 (S.D.) ml when inspiration time was 30% of the cycle to a mean of 605 $\pm$ 26 ml when an inspiration time of 70% of the cycle provided more time for gas mixing to occur.

A similar result was obtained when ventilation was increased. Bake and co-workers (1974) and Robertson and his colleagues (1969) have demonstrated that a more even distribution of ventilation results when inspiratory flow rate is increased. Thus, with increased frequency, better gas mixing, and, hence, a larger calculated FRC would be predicted. In the lower ventilation/volume range (below 10 (ml/min)/ml), this was the case (Fig. IV-6).

Increased ventilation resulting from larger tidal volumes enhance gas mixing more than a similar ventilation increase resulting from frequency changes (Young et al., 1968). The better mixing could be due in part to the influence of decreased mean airway resistance

accompanying a larger mean lung volume on convective and diffusive mixing and to the larger volume of fresh gas that enters the resident gas volume. The result of better gas mixing would be a corresponding larger calculated end-expiratory volume as shown in Figure IV-6.

Data obtained when PEEP was imposed on the animal provides a way of assessing the influence of mean lung volume on Krypton-81m mixing with resident lung gas. Figure IV-7 illustrates what would be predicted with and without improved distribution of gas accompanying an end-expiratory volume increase. If, in this model, the tidal volume was distributed throughout essentially the same volume before and after PEEP, the same fraction of the true end-expiratory volume would be calculated. If mixing was enhanced, the calculated value would provide a better estimate of the true value. By imposing 10 cm H_2O PEEP, we increased the end-expiratory volume by 51% from 943 $\pm$ 133 (S.D.) ml to 1425 $\pm$ 182 ml. Although ventilation was held constant, the end-expiratory volume calculated on the basis of the gated analysis increased by the same proportion from 518 $\pm$ 88 ml to 772 $\pm$ 171 ml. Hence, we conclude that increasing resident volume did not alter Krypton-81m mixing with the resident volume significantly.

Extending this model to the case where an increased tidal volume occurs indicates that, the estimate of FRC would actually be less than that obtained with the smaller tidal volume unless better gas mixing accompanied the tidal volume change.

Data presented in Figure IV-5 suggests that a gas mixing limit may be reached beyond which further ventilation increases do not enhance mixing. Since the higher ventilation rates in this study were achieved by increases in frequency, however, this trend may reflect only a limit

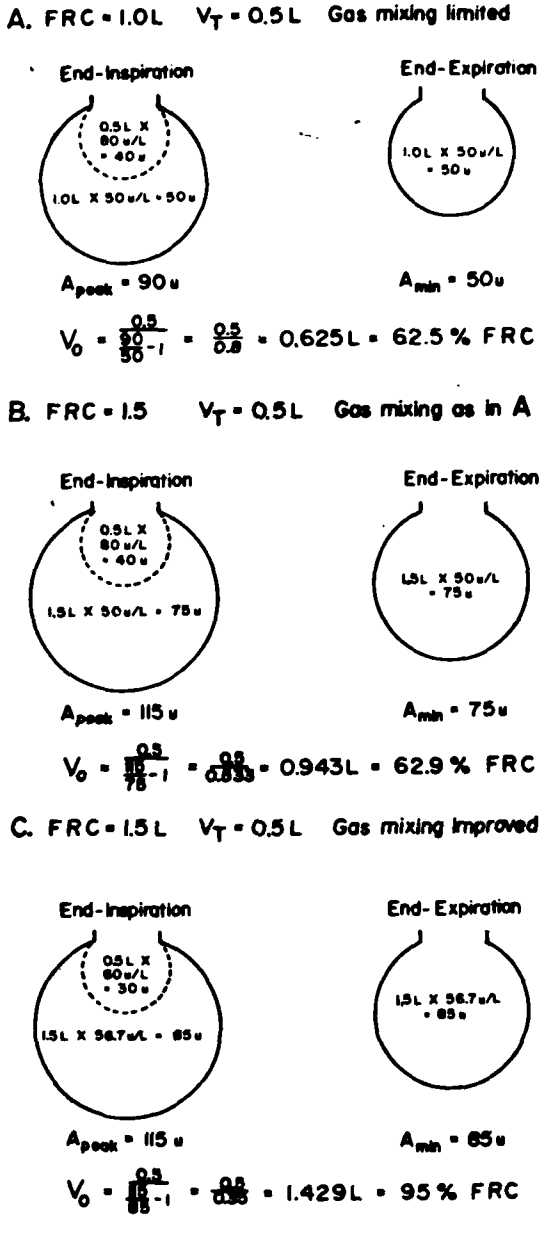

Figure IV-7. Model illustrating end-expiratory volume calculated if initial resident volume with hypothetical maldistribution (panel A) was increased with no gas mixing improvement (panel B) or increased with a concomitant increase in gas mixing (panel C).

associated with flow rate increases.

Data from the static acquisitions shown in Figure IV-2 do not indicate a dependence of Krypton-81m activity on ventilation mode. This does not contradict the gated analysis. The static acquistion represents a time-averaged indication of activity over the lung. When expressed as activity, the data reflect the quantity of Krypton-81m reaching the lung rather than distribution of that activity. The quantity of tracer reaching the lung is determined by volume per time delivered and the Krypton-81m quantity per volume delivered. Hence, for a given ventilation, the same activity level relative to inspired gas activity would be reached regardless of the tidal volume-frequency combination.

The inhomogeneity of Krypton-81m distribution and its dependence on factors such as tidal volume-frequency combination and inspiratory time could explain the differences between the experimental data and theoretical curves generated from a single compartment, well-mixed model (Fig. IV-3). In a single compartment, well-mixed model, the distribution volume of the tracer used to calculate concentration is the compartment volume. In the lung, however, this is not the case. The effective distribution volume of the Krypton-81m depends upon a number of variables, and it changes during the course of a breath. Hence, the single compartment, well-mixed model is not a good predictor of Krypton-81m behavior in the lung.

Use of Krypton-81m in lung imaging may, in fact, provide more information than the single compartment model suggests. When used in conjunction with Xenon-133 or other tracers allowing determination of regional lung volume distribution, quantitative information regarding

distribution of ventilation and the extent of further mixing of inspired and resident lung gas may be obtained. Use of the gated imaging technique with Krypton-81m and and a longer lived isotope may provide a means of quantitating gas mixing during the respiratory cycle.

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Publications

The following publications will arise from work begun during this contract.

1. Modell, H.I. Influence of G-suit abdominal bladder inflation on gas exchange during acceleration (+Gz). To be submitted to J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.

2. Modell, H.I. and F.W. Baumgardner. Interaction of chest wall and lung mechanics during +Gz stress. To be submitted to J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.

3. Modell, H.I. and M.M. Graham. Validity of basic assumptions in use of Krypton-81m for ventilation scans. To be Submitted to J. Nucl. Med.

4. Modell, H.I. Where should mixed venous blood be sampled? To be submitted to J. Appl. Physiol.: Respirat. Environ. exercise Physiol.

5. Modell, H.I. and J. Mendenhall. A pump system for remote blood sampling. To be submitted to J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.

Professional personnel associated with research effort

Harold I. Modell. Research Assistant Professor, Dept. Physiology and Biophysics

Michael M. Graham, Assistant Professor, Division of Nuclear Medicine

Interactions

Papers relating to this research effort have been or will be presented at the following meetings:

Review of Air Force sponsored basic research in environmental and acceleration physiology, 2-4 October 1979, St. Louis, Missouri

Modell, H.I. Effects of anti-G measures on gas exchange

FASEB, 13-18 April 1980, Anaheim, California

Graham, M.M. and H.I. Modell. Validity of basic assumptions in use of Krypton-81m for ventilation scans. Fed. Proc. 39: 1090, 1980.

Review of Air Force sponsored basic research in environmental and acceleration physiology, 23-25 September 1980, Lexington, Kentucky

Modell, H.I. Effects of anti-G measures on gas exchange

Modell, H.I. Use of Krypton-81m for continuous ventilation distribution

28th Annual Meeting of the Society of Nuclear Medicine, 16-19 June 1981, Las Vegas, Nevada

Graham, M.M. and H.I. Modell. Limitations of Krypton-81m use for ventilation scans

1981 Fall Meeting of the American Physiological Society, 11-16 October 1981, Cincinnati, Ohio

Modell, H.I. Effects of acceleration (+Gz) on the intrapleural pressure gradient